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STUDIES ON A CASE OF PORPHYRIA CUTANEA TARDA.

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PHOTOSENSITIVITY is not uncommon among dermatological patients, but in relatively few cases is the photosensitizing substance identified and the factors responsible for its appearance established. That porphyrins are photodynamically active and may lead to severe clinical photosensitization has been recognized for some time. Günther (1922) in his early work on the porphyrias described as *porphyria congenita* a relatively rare familial disease in which photosensitivity was present from birth, and was accompanied by the deposition of porphyrin in the bones and teeth and by the excretion of large quantities of porphyrin in the urine. Later studies by Borst and Königsdörffer (1929) on the pathological side, and by H. Fischer and his collaborators (1925) on the chemical side, added much to our knowledge of the condition. The urinary porphyrins were recognised as uroporphyrin (containing 8 carboxyl groups) and coproporphyrin (containing 4 carboxyl groups), and the effect of these upon animals and micro-organisms was studied in the absence and in the presence of light. A personal study by Meyer-Betz (1913), who injected 200 mg. of haematoporphyrin (a chemically prepared dicarboxylic porphyrin) intravenously into his own arm, left no doubt about the powerful photosensitizing properties of this group of substances.

During recent years it has become apparent that several forms of porphyria or several distinct diseases of porphyrin metabolism exist. A classification was introduced by Waldenström in 1937 to supersede the earlier ones of Günther and others. This included three main types : (*a*) the porphyria congenita of Günther, (*b*) porphyria acuta, and (*c*) porphyria cutanea tarda. In the last group he placed cases in which increased urinary porphyrin excretion and photosensitization developed later in life, and in which a sclerodermic tendency was

noticeable. The occurrence of colic, similar to that of acute porphyria, and the occasional excretion of uroporphyrin in the urine was noticed by Waldenström, but at that time nervous symptoms had not been observed in these cases.

Still more recently Gray, Rimington and Thomson (1948) and Macgregor, Nicholas and Rimington (1952) have called attention to a biochemical feature which appears to be characteristic of porphyria cutanea tarda (Rimington, 1952); this is the excretion during remission periods of large quantities of porphyrin (mainly protoporphyrin and coproporphyrin) in the stool and a fall in this level during attacks or exacerbations when the urinary porphyrin rises (mainly uroporphyrin and coproporphyrin). Porphyrin is detectable in the plasma and photosensitivity becomes more severe during attacks. From determinations of stool porphyrins in patients exhibiting intermittent photosensitivity but normal urine chemistry, one of us (C. R.) has detected several new examples of this syndrome.

Not all observed cases of porphyria cutanea tarda have suffered from attacks of abdominal colic or nervous involvement, and it is difficult to say whether the disease may begin in a simple manner and become progressively more complex, or whether a further subdivision is needed into cases which remain stationary and those which progress. There would appear to be some chemical differences between the two types (Nicholas and Rimington, 1953). Some degree of hepatic damage appears to be a frequent accompaniment of porphyria cutanea tarda, and attention may be drawn to the description of what is termed "porphyria hepatica" by Watson (1951) and to the major role of alcoholism in the series of cases of "chronic porphyria" reported by Szodoray and Sümegi (1944) and by Brunsting *et al.* (1951).

Recent investigations employing the techniques of radioactive labelling have made it almost certain that biosynthesis in the erythropoietic tissue of the bone marrow leads primarily to uroporphyrin, which is then partly decarboxylated, yielding coproporphyrin, and this, in turn, is transformed to protoporphyrin by further loss of two carboxyl groups and simultaneous oxidation.

In each of the pathological conditions just considered there is an abnormally large excretion of porphyrins and the consensus of opinion is that this is due to increased, and possibly disordered, synthesis. In congenital porphyria the bone marrow is regarded as the site of over-production, but with regard to acute porphyria and porphyria cutanea tarda opinions differ. Watson (1951) considers that the liver is principally concerned, but it is not clear whether he regards the porphyrins as arising by synthesis or by degradation, and if the former, which cells are responsible for their production. Much more data need to be accumulated before the chemical pathology of these diseases is fully understood.

In 1951 a man came to the out-patient clinic at University College Hospital complaining of an eruption during the past five years on the parts of the skin

exposed to sunlight. He proved to be a case of porphyria cutanea tarda, and this paper records a study carried out upon him during the past two years.

Case Report.

Mr. L. M—, aged 30 in 1951, a draughtsman and printer, intelligent and co-operative, had enjoyed good health apart from a mild attack of jaundice lasting 5 weeks in 1944. He served in the Royal Air Force from 1946–8 but was never abroad. Before his present trouble, he used to work much in the sunlight and had no reaction to it apart from occasional ordinary sunburn. He has not had any abdominal pains or nervous trouble. He had been in the habit of drinking regularly about 17 pints (9·6 l.) of beer each week, but he has now reduced his consumption to about 8 pints per annum.

Neither of his parents has experienced light sensitivity and they are not blood relatives. He has a brother (S. M—) aged 37, found to be normal, and a sister (G. M—) aged 22, who has a condition similar to that of our patient although less severe (see below). L. M— has two children who appear to be normal.

Present illness.—In 1946 he had his first attack of light sensitivity. After an hour's exposure to bright sunlight his face began to tingle and later became swollen. Whiteness and swelling lasted for about a week, and the condition was quite different from ordinary sunburn. He had no further trouble until the summer of the same year, when on two occasions he had a similar reaction to direct sunlight. Again in the summers of 1947 and 1948 he had several attacks in which the face and backs of his hands were affected. In 1949 he had six attacks ; the reaction occurred after shorter exposure to sunlight (about 10 minutes) and was more severe. About two days after exposure, when the swelling was still present he noticed on the upper part of his face small yellowish crusts which gradually healed with scarring. In 1950 attacks were so frequent during the summer that his face was never free from either swelling or scabbing. On some occasions he reacted to bright light when the sun was behind cloud, and sometimes to sunlight through window glass. In 1951 his first attack came in April after a little week-end gardening, and during 1952, which was not an exceptionally sunny summer, he suffered more severely and almost continuously.

Besides the light-sensitive eruption, he has noticed during the past two years that minor traumata to the back of his hands result in exaggerated abrasions, and sometimes bullae, leaving slowly-healing ulcers followed by pigmentation. He states that his bowel action has always been normal. During interrogation in January 1953 he described an ache in the right hypochondrium tending to spread up the right side of his chest. This pain has been occurring about two or three times a week, beginning in the evening and passing off by morning.

On examination.—When first seen (1951) his skin was clear of active lesions. His forehead (Fig. 1) showed pigmentation, thickening and deep wrinkling, and there were small scars on the forehead, nose, ears and on the backs of the hands. At other times we have seen him with gross oedema or with blisters or ulcers on the face and backs of the hands. His skin and teeth gave no fluorescence under Wood's light.

General physical examination was negative. Skiagrams of the chest, sinuses and teeth were normal.

Haematology.—Hb 108% ; W.B.C. 8600 (Polys. 58%, lymphos. 34·5, monos. 4·5, eos. 3·0%). E.S.R. 11 mm. in 1 hour (Westergren). W.R. negative.

Serum proteins, electrophoretic pattern normal. Cephalin flocculation negative. Colloidal red, negative. Thymol turbidity 1 unit. Van den Bergh, direct, 1·2 mg. ; indirect *nil*. With ultra-violet light the serum showed red fluorescence estimated to correspond to about 0·69 mg. porphyrin/l.

The *urine* contained about 2·3 mg. of total porphyrins in 24 hours, of which about one-half was coproporphyrin. It has always been about normal in colour and in constituents other than porphyrin. Porphobilinogen has never been observed, and no abnormal amino-acids were found by filter-paper chromatography.

The *faeces* contained an excess of coproporphyrin and large amounts of protoporphyrin.

FIG. 1.—The patient when first seen in 1951. The face is free from active lesions. The forehead shows scarring, pigmentation and thickening of the skin.

INVESTIGATIONS.

Normal diet.—Porphyrin excretion was studied during two short stays in hospital. Faeces were collected between markers (carmine) spaced 3 days apart, and 24-hour outputs of urine were saved at the same times. Urinary uroporphyrin was determined by the method of Rimington and Sveinsson (1950) and coproporphyrin by acetic-acid-ether extraction followed by spectrophotometry in 0·1 N–HCl solution. Ether-soluble faecal prophyrins were extracted in the same way from an aliquot of the homogenized material, and coproporphyrin and protoporphyrin fractions separated by shaking with 0·1 N and 1·4 N–HCl respectively. Porphyrin in these extracts was determined spectrophotometrically. The faecal residue was examined for ether-insoluble por-

phyrin by digestion with methanolic HCl, and spectrophotometry after transference to $CHCl_3$ of any porphyrin esters present.

Qualitative identification of the types of porphyrin present in each extract was made by paper chromatography using the lutidine-water system (Nicholas and Rimington, 1949, 1951) after preliminary purification upon MgO columns (Nicholas, 1951).

The results of these investigations are included in Table I, from which it will be seen that on ordinary hospital diet the patient excreted about 50 mg./day of total porphyrin in his stool and about 2 mg./day in the urine; normal figures are 0·15–0·35 mg. (mainly coproporphyrin) and 0–0·1 mg. (coproporphyrin) respectively per day. Exposure to the sun on two days possibly caused a slight increase in porphyrin excretion (Table I).

The stool porphyrin consisted mainly of protoporphyrin, the dimethyl ester of which was prepared and crystallized (m.p. 221°, α–band in $CHCl_3$ 630·8 mμ), together with smaller quantities of mesoporphyrin (ester m.p. 206–8°, α–band 621·0 mμ.) and relatively little coproporphyrin. A tri-carboxylic porphyrin was detected by paper chromatography but could not be isolated owing to its instability.

In the urine porphyrins with 8, 5, 4 and 2 carboxyl groups respectively were present. The coproporphyrin was predominantly the series III isomer and had ester m.p. 144°, remelt 166–8°.

Vegetable-free and meat-free diets.—The possibility existed that some or most of the porphyrins present in the stool might have been derived directly from pyrrole pigments in the diet and have not been truly endogenous products. All green vegetables were excluded from the diet for 5 days and then both vegetables and meat were excluded for the next 8 days and porphyrin elimination was determined (Table I). This was during the second period in hospital, 4 months after the first, and it will be seen that exclusion of vegetables and meat made no significant difference to the output of porphyrins.

Duodenal intubation.—To gain further evidence concerning the endogenous nature of the porphyrins in the stool, a duodenal tube was passed and a mixture of resting stomach juice and bile was aspirated. After injection of a little magnesium sulphate solution down the tube, several specimens of bile were collected over 10 minutes. The analyses recorded in Table II show quite conclusively that the bile was the source of the porphyrin found in the stool.

Administration of riboflavin.—Stich and Eisgruber (1951) have reported that yeasts cultured on media deficient in riboflavin produce considerable quantities of the abnormal coproporphyrin I, and that this is replaced by coproporphyrin III on the addition of riboflavin to the culture fluid. There have also been claims that cases of acute porphyria are benefited by riboflavin (Vannotti, 1940). These observations prompted us to examine the effect of riboflavin administration on our patient whilst on an ordinary mixed diet. He received 54 mg./

TABLE I.—*Urinary and Faecal Excretion of Porphyrins by L. M—.*

Date.	Treatment.	Urine. Coproporphyrin (mg./l.).	Urine. Coproporphyrin (mg./day).	Urine. Total porphyrin (mg./l.).	Urine. Total porphyrin (mg./day).	Faeces. Protoporphyrin (mg./day).	Faeces. Protoporphyrin (mg./g. dry).	Faeces. Coproporphyrin (mg./day).	Faeces. Coproporphyrin (mg./g. dry).
1951.									
May 28/29	None	1·540	1·830	1·955	2·326	—	—	—	—
,, 30/31	—	1·069	1·410	1·713	2·262	50·81	1·58	3·24	0·10
31/June 1	—	1·090	1·416	1·792	2·330	—	—	—	—
June 1/2	Exposed to sun	1·064	1·830	1·947	3·349	—	—	—	—
,, 2/3		1·397	1·481	2·500	2·650	—	—	—	—
Sept. 23/24	Vegetable-free diet	0·851	—	No uroporphyrin		—	—	—	—
,, 24/25		0·703	—	—		44·10	2·47	0·96	0·05
,, 25/26	Vegetable- and meat-free diet, Sept. 25 to Oct. 2	1·133	—	—		—	—	—	—
,, 28/29		—	—	—		—	—	—	—
,, 29/30		—	—	—		68·60	2·03	2·33	0·07
,, 30/Oct. 1		0·925	—	No uroporphyrin		—	—	—	—
Oct. 1/2		—	—	—		—	—	—	—
,, 15	Riboflavine 54 mg./day from Oct. 8–22	5·06	—	0·19 (protop.)		102·8	1·83	8·74	0·16
,, 19/20		2·03	2·13	—		—	—	—	—
,, 20/21		2·28	1·93	—		74·15	2·78	5·34	0·20
,, 21/22		2·40	1·81	—		—	—	—	—
Nov. 18/19	Vit. B_{12} (50/μg.) on Nov. 12, 14, 16	1·33	1·46	No uroporphyrin		—	1·30	—	0·03
1952.									
Jan. 14	—	0·332	0·382	—		—	1·443	—	0·109
April 28	None	0·642	—	—		—	1·283	—	0·178
,, 29	Aureomycin 0·25 g. 8 times a day for 7 days. Stool collection on 7th day	1·034	—	—		—	1·066	—	0·188
1953.									
Jan. 15	—	1·824	—	0·182 (protop.); no uroporphyrin		—	—	—	—

(Where stools were collected between markers, the dates are indicated by a bracket.)

TABLE II.—*Porphyrin Content of Fluid Samples Obtained from L. M— by Duodenal Intubation and Use of Magnesium Sulphate* (Oct. 1951).

No.	Vol. (ml.).	Porphyrin (μg./ml.).	Porphyrin (Total μg.).	Remarks.
1	9	14·73	132·5	"Resting" duodenal juice. Turbid.
2	10	5·40	54·0	,, ,, ,, Clear.
3	10·5	3·11	32·6	1st after introduction of mag. sulph. Pale; turbid.
4	3·2	18·54	59·3	2nd after introduction of mag. sulph. Clear and practically pure bile.
5	8·5	3·40	28·9	3rd final sample; clear.

Note.—At the time of this experiment the serum had a bright red fluorescence in ultra-violet light and bilirubin content of 0·5 mg. %. The porphyrin in these samples of duodenal fluid was almost entirely protoporphyrin, but uroporphyrin was also detected chromatographically.

day for 3 weeks; urines were collected daily and faeces weekly. The results in Table I show that both urinary and faecal porphyrin output were increased during this trial, Hepatic excretory function may have been improved, but there was certainly no diminution in the total porphyrin produced (Table I).

Administration of vitamin B_{12}.—Some observations of Pimenta de Mello (1951) led us to try the effect of this vitamin upon our patient. He was given 50 μg. of B_{12} intramuscularly on 12, 14 and 16 November and his faeces and urine were collected during 18–19 November. The porphyrin excretion was not significantly altered during this period or when redetermined 2 weeks later (Table I).

Administration of aureomycin.—It was thought that sterilization of the gut with aureomycin would provide further evidence concerning the origin of the faecal porphyrin in this patient. Two trials were carried out, but the first was spoilt by intolerance to the drug with digestive upsets. In the second trial he received 2 g. daily for 7 days. The stool was odourless, but on analysis both it and the urine contained as much porphyrin as in the control pre-dosage period (Table I).

Identification of Serum Porphyrin.

The patient's serum at this time showed pronounced red fluorescence in ultraviolet light. Attempts to isolate the porphyrin in sufficient quantity and in suitable form for identification were unsuccessful. An alternative possible method of identification was the comparison of the fluorescence spectrum exhibited by the serum with the spectra given by sera containing known porphyrins. This was accomplished through the co-operation of Dr. Holiday of the M.R.C. Spectroscopic Unit, London Hospital. To specimens of human serum were added solutions in dilute sodium carbonate of protoporphyrin, coproporphyrin and uroporphyrin respectively, in quantity sufficient to give a fluorescence comparable in intensity with that of the patient's serum. Uroporphyrin and coproporphyrin both afford two emission lines, but protoporphyrin gives only one, as also did the patient's serum. The conclusion may be drawn therefore that the main porphyrin present in the patient's serum is the same as that predominating in the bile and faeces, namely protoporphyrin. The quantity was judged to be at this time about 0·69 mg./l.

Light Sensitivity Tests.

Light sensitivity tests were carried out at various times commencing with his first admission to hospital. One inch squares on the dorsa of the wrists were irradiated as follows.:

(i) Mercury vapour "Alpine" lamp at 18 in. for 30 seconds (the usual erythema dose with this lamp).

(ii) "Sollux" radiant heat and light at 18 in. for 10 minutes.

(iii) Photoflood lamp (300 watt) at 18 in. for 10 minutes and for 60 minutes.

(iv) Kromayer lamp. minimal erythema dose without filters, and longer exposures through Wood's glass, and glass slides. With none of the above light sources was there any reaction of the skin of any kind.

On 1 June 1951 the patient exposed the back of his right hand to direct sunlight for 20 minutes (at 5·30 p.m. in London). Tingling had already been noted during the exposure, and after 4 hours the hand was grossly oedematous. By the next day the back of the hand showed both pitting oedema and purpura.

The back of the left hand was then exposed to sunlight, after having been smeared with a vanishing cream containing 4% tannic acid Ten minutes'

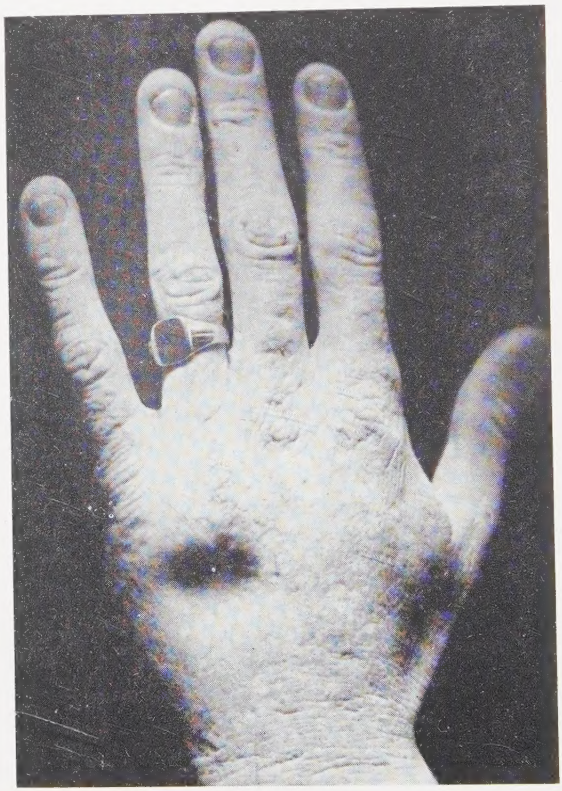

FIG. 2.—Dorsum of left hand two days after exposure to sunlight, showing pitting oedema.

exposure to direct sunlight produced a severe oedematous reaction, and after 48 hours pitting oedema was still present (Fig. 2). After 3 days oedema of the right hand had largely subsided, but there was still purpura.

Later in the season he exposed a hand to sunlight through window glass, and after 45 minutes there was a tingling in the skin, which was a little oedematous the next day.

About this time (October 1951), the patient described how the " ammonia " printing process that he used at work required an enclosed carbon arc lamp. He would be exposed to this for short periods of about a minute at a time but

with an aggregate of about 10 minutes during a day's printing. This lamp burns in an atmosphere poor in oxygen and gives out a very powerful light in the blue, violet, and very near ultra-violet regions, its main emission being between

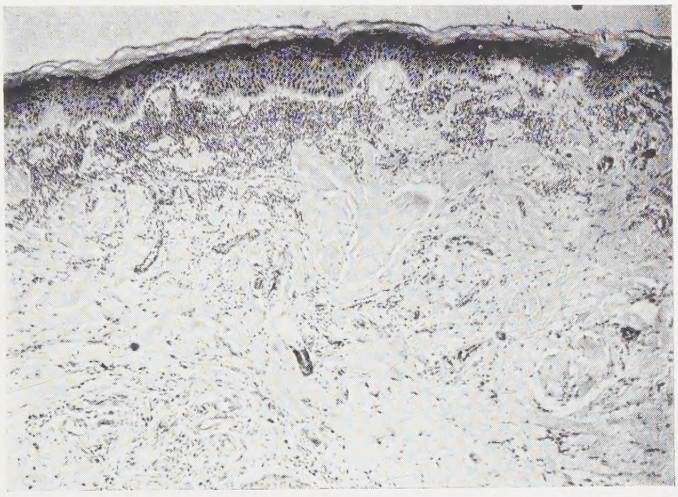

FIG. 3.—Biopsy from dorsum of right hand 3 days after exposure to sunlight. In subpapillary corium, note extravasation of red cells and hyaline connective tissue changes. H. & E.

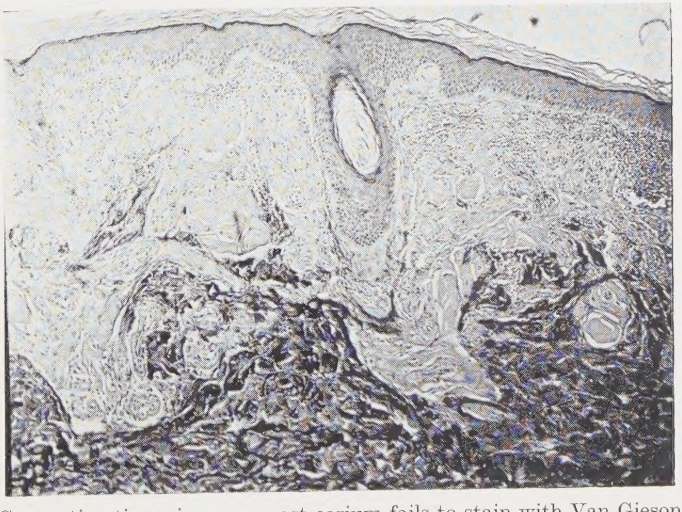

FIG. 4.—Connective tissue in uppermost corium fails to stain with Van Gieson. Deeper collagen fibres are the normal red colour. Van Gieson.

3500 and 4100Å. The patient exposed part of the back of his right hand to the enclosed carbon arc lamp for 15 minutes at 15 in. distance. There was a tingling sensation and the hand swelled up, and by the next day we observed gross oedema and purpura just as after sunlight. He persuaded a workmate,

a normal subject, to expose his hand to the same arc lamp in the same manner for twenty minutes, but in his case there was no skin reaction.

A biopsy was made from the dorsum of the patient's right hand after the

FIG. 5.—Thickening and dark staining of capillary walls with periodic acid-Schiff stain.

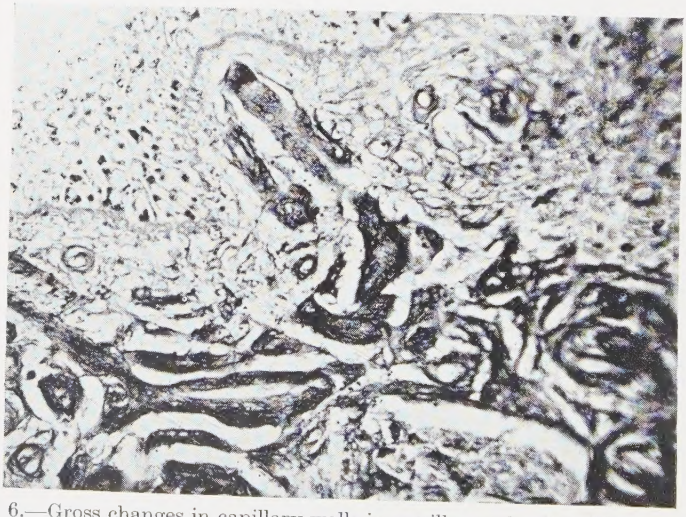

FIG. 6.—Gross changes in capillary walls in papillae and subpapillary corium. Periodic acid-Schiff.

acute swelling following exposure to sunlight had subsided but while it was still purpuric, immediately before the photograph (Fig. 2) was taken. Histological findings were as follow : In the upper corium there is extravasation of red cells around the capillaries, and the connective tissue shows hyaline changes

(Fig. 3). With Van Gieson stain deeper collagen tissue fibres appear normal, but in the upper corium connective tissue fails to stain red (Fig. 4); there is however, no increase of elastic staining, the elastic fibres being pushed aside by the hyaline masses. With periodic acid-Schiff stain it can clearly be seen that there is intense staining of the greatly thickened ground substance of the vessel walls in the papillary and subpapillary corium and oedema beyond the vessel walls (Fig. 5 and high-power detail of capillaries in Fig. 6).

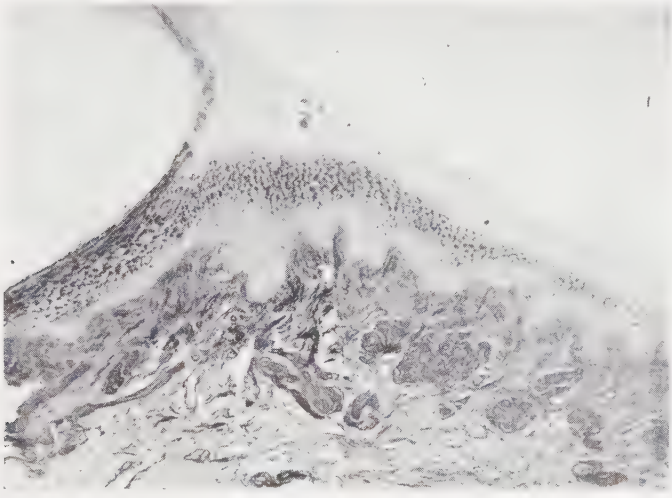

FIG. 7.—Biopsy of traumatic bulla on back of hand. The bulla is intra-epidermal. There is large accumulation of glycogen in the mid-epidermis. Gross thickening of walls of capillaries in uppermost corium. Periodic acid-Schiff.

Later, a biopsy was made from a small traumatic vesicle on the back of the right hand, at a time when there had been no exposure to sunlight for several weeks. The histological sections show an intra-epidermal vesicle with no inflammatory reaction in or below it. There is a considerable accumulation of glycogen in the mid-epidermis (Fig. 7), and with periodic acid-Schiff stain one can still see the extraordinary changes in the walls of the capillaries in the uppermost corium.

INVESTIGATIONS ON THE PATIENT'S RELATIVES.

Brother S. M- -, aged 37, clinically normal: this subject excreted normal amounts of porphyrin in his urine and faeces (Table III).

Daughters: The patient's twin daughters aged 2 years showed normal urinary and faecal porphyrin excretion (see Table III).

TABLE III.—*Urinary and Faecal Excretion of Porphyrins by Relatives of the Patient, L. M—.*

Date.	Relative.	Urine.		Faeces.	
		Coproporphyrin (mg./l.).	Other porphyrins (mg./l.)	Protoporphyrin (mg./g. dry wt.).	Coproporphyrin (mg./g. dry wt.).
Apr. 1952	V. M— (daughter aet. 2)	0·042	—	0·011	0·006
,,	J. M— (daughter aet. 2)	0·045	—	Total 0·032	
June 1951	G. M— (sister aet. 22)	0·047	—	1·270	0·045
Oct. ,,	—	0·037	—	—	—
Jan. 1953	—	0·328	Protop. 0·016 ; no uroporphyrin	—	—
Nov. 1951	S. M— (brother aet. 37)	0·037	—	0·018	0·009

Sister G. M—, aged 22.

Case History.—Her general health had been entirely satisfactory until 1948 when she started to get reactions from exposure to bright sunlight. The first occasion was while at the seaside in July when the unprotected dorsa of hands and feet and the ankles became swollen after exposure. Further isolated attacks occurred in the summers of 1949 and 1950 when besides the hands, the face also became swollen. In April and May 1951 similar attacks developed after less exposure to sunlight than formerly, these occurring in London and earlier in the year. The eyes have become completely closed by swelling; if she avoids the sun the attacks subside in about a week. About one hour's exposure to sunlight is required to bring on an attack. Her skin is unduly sensitive to trauma, and she often finds she has lesions on the face in the morning as a result of friction from curlers. She has experienced two attacks of abdominal pain and of "indigestion" lasting a few weeks, the first being in January 1950 the more recent one in early 1951, but we have not yet had an opportunity of investigating these symptoms. She drinks seldom, taking only a little spirits at times such as Christmas.

When seen in May 1951 there was no gross swelling of the face, but there was some pigmentation of the upper part of the forehead; there were three scars on the nose, and one from a blood blister that she had had on the hand during last year's attack. The scars resemble those of our patient L. M—, her brother. Her serum exhibits a faint red fluorescence.

Specimens of urine examined in June and October 1951 showed no abnormality of porphyrins or of amino-acids, but specimens of faeces were found to contain quantities of porphyrins as great as those excreted by her brother L. M— (Table III). When tested in January 1953 her urine was found to contain 328 μg./l. of coproporphyrin—a quantity well above the normal maximum.

Discussion.

The photosensitivity manifested by our patient L. M— and by his sister G. M— seems to be referable to an abnormal production of porphyrins (mainly protoporphyrin) which are largely excreted in the stool, *via* the bile, and to the presence of similar porphyrins in the blood plasma. These cases we regard as examples of porphyria cutanea tarda. L. M— has a history of a mild attack of jaundice of 5 weeks' duration in 1944. His serum bilirubin was 1·2 mg. % when determined in 1951 and he has been a moderate drinker. While under observation his general health has remained satisfactory, but there was one incident of abdominal and low back pain lasting a few days. Unfortunately we were unable to get any excreta at that time.

His sister G. M— has had two attacks of abdominal pain and indigestion lasting a few weeks in 1950 and 1951. Neither subject has experienced any nervous disorder. Both have noticed a hypersensitivity of the skin to trauma, and histological examination of L. M— has revealed certain interesting defects. We have demonstrated that his faecal porphyrins are derived from the bile and not from microbiological activity in the gut. Photosensitization has been demonstrated experimentally by exposure to radiation of suitable wavelength. The failure with other artificial sources of light is probably attributable to lack of sufficient radiation in this particular spectral region. It should be noted that the patient reacts to sunlight through window glass, that tannic acid failed to protect him against sunlight, and that the absorption band of porphyrins comes within the range of the light to which he reacts (around 4000Å).

It would appear that in L. M— mild alcoholism may have been responsible for a degree of hepatic insufficiency associated with his greatly increased porphyrin production, but in the case of his sister G. M— this hypothesis is not applicable. In both patients the condition seems to be progressing from a simple cutaneous manifestation to a disease in which intermittent attacks of colic occur as in acute porphyria. Whether nervous manifestations will also make their appearance in time cannot be stated ; but the case may be recalled of a boy studied by Macgregor, Nicholas and Rimington (1952) in whom a similar progression culminated in a relatively short time in a fatal attack in every way simulating acute porphyria in relapse.

It is our belief, however, that the two diseases, acute porphyria and porphyria cutanea tarda, are quite distinct both pathologically and biochemically. We never accept as acute porphyria any case showing photosensitization or bulla formation, and endeavour always to make a determination of stool porphyrins during remission.

Porphyria cutanea tarda shows points of similarity with congenital porphyria but these are only superficial. Attacks of abdominal colic do not occur in

congenital porphyria, and there is in this disease a steady output of considerable quantities of porphyrin (mainly series I isomers) in the urine.

It is of much interest that we have studied two cases of porphyria cutanea tarda in the same family, for this suggests that the disease may be a gene-controlled metabolic abnormality as in the case of the other porphyrias. Brunsting and Mason (1946) refer to a latent case in the sister of a patient ; otherwise genetic data are very scanty, especially if one considers only cases in which the diagnosis has been established beyond doubt. The fact that the urinary porphyrin excretion departs so little from the normal in porphyria cutanea tarda in remission suggests that many cases of photosensitivity of unestablished origin and perhaps some cases labelled epidermolysis bullosa may in reality be examples of this derangement of pyrrole pigment metabolism.

The histological changes in skin lesions of porphyria have usually been described as non-specific, although Brunsting and Mason in one of their cases (1949) noted and illustrated changes, somewhat resembling colloid milium, which in fact look very like the lesions we are describing.

Our histological finding of extreme swelling of the capillary walls in the uppermost cutis is, as far as we are aware, an original observation. The change resembles superficially the "senile" connective-tissue changes of exposed skin, but in our case the amorphous material does not take up elastic tissue stain, and the periodic acid-Schiff stain brings out the details showing that the main effect is swelling and intense staining of the basement membrane of the capillaries. We also had the opportunity of examining a small traumatic blister, and here we found the lesion to be intra-epidermal. Even though there had been no recent swelling of this hand when the biopsy was taken, the capillaries of the upper corium still showed the remarkable basement membrane changes described above. The small blisters and abrasions produced by minor traumata resemble the lesions of epidermolysis bullosa, but are probably quite distinct therefrom ; Brunsting and Mason (1949) suggested the term "bullosis actinica et mechanica" for this type of lesion. As far as we know such lesions appear only in skin previously damaged by light, and perhaps the capillary changes which we have described contribute to the fragility of the upper layers of the skin.

The light which causes eruption of the skin is certainly of a quality that could penetrate to the vessels of the upper corium, and a photo-reaction due to porphyrins might take place there. A vascular basis has been suggested as an explanation of the minute lesions seen in various types of porphyria, though the exact mechanism remains obscure. Gaffron (1926) and others have, however, demonstrated a photo-oxidation of protein in the presence of porphyrins. Feldberg (1952) has recently brought forward evidence for the local liberation of histamine during haematoporphyrin photo-sensitization reactions in rats and rabbits. The peculiar damage to the capillary walls of the skin

in our case may be of some general significance, and it may be noted that after the application of an arm cuff the patient developed purpura in sites that had been previously irradiated but not in other areas of the same arm.

Summary.

1. A case is described of pophyria cutanea tarda with recurrent eruption of the exposed skin, particularly in the summer. There is abnormality of porphyrin excretion (about 50 mg. daily in the stool and 2 mg. daily in the urine), but, apart from recent complaints of rather vague abdominal pain, no other abnormality. The patient has a sister with a similar condition and a brother who is normal. The patient's twin daughters are normal.

2. No marked change in porphyrin excretion followed exclusion of green vegetables, or of green vegetables and meat from the diet, or the administration of riboflavin, vitamin B_{12} or aureomycin.

3. The bile was shown to have a high porphyrin content, thus supporting an endogenous origin for these pigments.

4. The patient's serum contains protoporphyrin.

5. The skin eruption of purpura and oedema was reproduced by sunlight, by sunlight through window glass, and by exposure to an enclosed carbon arc lamp with a very high emission between 3500 and 4100Å.

6. Histological sections of exposed skin showed gross hyaline swelling of walls of capillaries in the upper corium, and periodic acid-Schiff stain revealed swelling and intense polysaccharide staining of the basement membrane, even when there had been no exposure to sunlight for several weeks. This damage to the minute vasculature may account for the abnormal fragility of the skin.

7. The pattern of porphyrin excretion in porphyria cutanea tarda and the relation of this disease to congenital porphyria and to acute porphyria are discussed in the light of findings in the present case.

We are very grateful to Dr. W. N. Goldsmith for referring the patient for investigation and for his interest in and help with the work at all stages. Our thanks are also due to Dr. P. Hare for recent follow-up studies on the family, to Dr. F. V. Flynn for much work in preparation of excreta for detailed study, to Dr. C. E. Dent for paper chromatography of urinary amino-acids, and to Miss P. Miles and Mr. F. Grover for technical assistance.

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CUTANEOUS MANIFESTATIONS OF PORPHYRIA: SOUTH AFRICAN CASES.

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IN the porphyrias, porphyrin is present in the tissues and is excreted in the urine and faeces in excess of the normal amounts. The porphyrin may be uroporphyrin or coproporphyrin and, in addition, there may be an excretion of porphobilinogen. Porphyria is an inborn error of metabolism, the porphyrins possibly being formed during the synthesis of haemoglobin, but there is diversity of opinion about this. Although all cases of idiopathic porphyria suffer from this inborn error, the disease may, nevertheless, remain latent until quite late in life.

Porphyrinuria occurs also in a variety of diseases apart from idiopathic porphyria, namely, in severe anaemias, especially pernicious and haemolytic anaemias, pellagra, hydroa aestivale, damage to the liver by poisons such as alcohol and lead, and after the ingestion of certain drugs among which are benzene, trional, arsphenamine, sulphonal, chloroform, sulphonamides, veronal, barbiturates, trinitrotoluene, aspirin, acetanilide, phenacetin, phenazone and amidopyrin.

Three main types of porphyria have been classified by Watson (1951).

1. *Congenital.*—In this type there are well-marked skin manifestations in the form of chronic erythematous and bullous eruptions, with exacerbations in spring and summer simulating hydroa aestivale. It is inherited as a Mendelian recessive, is commoner in males and occurs pre- or post-natally, with marked photosensitivity. Nikolsky's sign may be positive, suggesting a resemblance to epidermolysis bullosa congenita. Neurological and abdominal symptoms are extremely rare. This type is sometimes associated with haemolytic anaemia. The urine is red at times, the bones and teeth are stained pink, and they all show a red fluorescence under near ultra-violet light.

2. *Acute.*—The acute type of porphyria has its onset later in life, with intermittent episodes of acute abdominal pain and neurological or mental symptoms as the predominant features rather than skin lesions or photosensitivity, which are very rare. It is inherited as a Mendelian dominant, commoner in females. The urine is red at times, and fluoresces, but there is no fluorescence or pink-staining of the bones and teeth. Porphobilinogen is characteristically present in all cases of acute porphyria.

3. *Chronic.*—This type, also called the "cutanea tarda" form, occurs in young adults and is an altogether milder syndrome. There may be cutaneous,

gastro-intestinal and occasionally neurological symptoms. Bullous eruptions, accompanied by pigmentation, hypertrichosis and milia appear on exposed surfaces, often following exposure to sunlight or trauma. Menstrual disturbances are frequently complained of, particularly amenorrhoea. The urine is red and fluorescent; there may be slight pink-staining and fluorescence of the bones and teeth. Porphobilinogen, coproporphyrin and uroporphyrin are present in the urine in varying amounts. These people tend to be constipated by habit.

During the last two years five cases of porphyrinuria with cutaneous manifestations have been seen in the Dermatological Department of Groote Schuur Hospital. They all had pigmentary changes in the skin; four of them had bullous eruptions on the exposed parts, and the fifth had mental symptoms associated with pigmentation of the face.

Case 1.—A Bantu man aged 44 years was first seen in the Dermatological Clinic in 1948 with pigmentation of the face and forearms which, he stated, had commenced in December 1947 while he was working out of doors as a labourer. In May 1950 he reappeared at the clinic and was admitted for investigation. At that time the skin condition had markedly deteriorated; on the face, neck, forearms and hands there were bullae, ulcers, induration and secondary sclerodermatous changes with contractures of the fingers and melanosis of the trunk. Many old lesions had healed with depigmented scars; the fresh lesions were badly impetigenized. On general physical examination nothing abnormal was found.

Laboratory investigations revealed coproporphyrin in the urine; a negative Wassermann reaction; grossly abnormal liver function (thymol turbidity 5·5; colloidal gold 4; thymol flocculation 2. Serum proteins: albumin 3·9 g. %; globulin 3·6 g. %).

He left hospital in September 1950 to resume his occupation as a labourer, but was unable to continue this for long because of the deformities of his hands. He was readmitted to the ward in September 1952 when it was found that the mutilations, contractures and ulcerations had greatly progressed. There were many pitted scars of healed bullae surrounded by rims of dark pigmentation. The fingers were bent, shortened and webbed together, simulating the late stages of epidermolysis bullosa. The skin of the face, neck and arms was extremely indurated and felt sclerodermatous. He showed no sensitivity to artificial ultra-violet light. The liver and spleen were not enlarged clinically, but the liver function tests were still abnormal (thymol turbidity 3·5; colloidal gold 3; thymol flocculation 3. Serum proteins: albumin 4·2 g. %; globulin 4·3 g. %). He refused liver biopsy. In the first 24-hour specimen of urine there was 9·6 mg. of coproporphyrin. There was a red-gold fluorescence of the urine, but not of the teeth, tongue or skin. In view of the marked induration of the skin a barium swallow skiagram was done; nothing abnormal was found. For a week he was given oral cortisone, which produced some improvement in the mobility of his wrists and fingers but no significant fall in the amount of urinary porphyrin.

Case 2.—A coloured woman aged 39 years was admitted on 1 September 1952, complaining of large bullae on the hands with pigmentation and hypertrichosis of the face of two months' duration. She had not taken either drugs or alcohol prior to the onset of the condition, nor had she noticed that exposure to sunlight or trauma

exacerbated the lesions. She had observed that her urine was a peculiar pink colour at times. There was no history of menstrual disorders.

On examination there were several large, flaccid bullae on the palms, with pigmentation over the joints of the fingers and wrists. Most of the face was darkly pigmented with a growth of fine, downy, black hairs on the pigmented areas. There was evidence of malnutrition in the follicular hyperkeratosis on the forearms and thighs, but no typical pellagrinous dermatosis. The liver was enlarged two fingers down and the liver function tests were abnormal (thymol turbidity 4; colloidal gold 2; thymol flocculation 2. Serum proteins: albumin 4·3 g. %; globulin 2·4 g. %).

Liver biopsy revealed an early diffuse cirrhosis with moderate excess of iron-containing pigment for the most part in the Kupffer cells, but also in portal tracts and parenchymal cells in some areas; there was no fatty change or necrosis. The urine contained coproporphyrin and uroporphyrin in amounts varying between 2·6 and 7·6 mg. per day.

Case 3.—A European woman aged 30 years was admitted to the ward on 17 September 1951. She had always been in good health until eighteen months before admission when she began to have severe metrorrhagia and menorrhagia, for which hysterectomy was performed in June 1951. At that time she was given many drugs, among which were nembutal, gelonida, pentothal and ether. One month after the operation she exposed herself to strong sunlight for a whole morning; that evening the face, hands, arms and lower legs became acutely red, oedematous and pruritic. These symptoms subsided after a few days, but the face was left markedly pigmented. Bullae began to appear on the fingers after mild trauma and she noticed a growth of fine, downy hairs on her face. There was nothing of note in her family history.

On examination the most striking feature was a marked brown pigmentation of the face, neck, hands and feet. The face was covered with fine downy light brown hairs. Several depressed scars of healed bullae were present, mainly on the forehead and cheeks. There were septic bullae on several fingers. Nikolsky's sign was positive. No significant abnormalities were found on general examination of the other systems.

The blood picture was normal; the sedimentation rate was 39 mm. (Wintrobe). The liver and spleen were not clinically enlarged but the liver function tests were abnormal (thymol turbidity 5·5; colloidal gold 3; thymol flocculation 3. Serum proteins: albumin 3·7 g. %; globulin 3·7 g. %). There was no fluorescence of the urine or of the tongue, but healed and fresh bullae on the hands and face showed a red-gold fluorescence under ultra-violet light. The urine contained increased coproporphyrin (200 μg. per 100 c.c.; 4·46 mg. in 24 hours); a trace of uroporphyrin was present, but there was no porphobilinogen.

Case 4.—A European woman aged 20 years was admitted in July 1950 complaining of blisters on the face and hands, which began to appear one month after an attack of infective hepatitis. She had had amenorrhoea for three months. She noticed that the vesicles appeared soon after exposure to sunlight. No other members of her family had had similar eruptions.

On examination there were numerous slightly pigmented scars on the face and on the hands, particularly over the joints of the knuckles and fingers. The liver and spleen were not clinically enlarged at the time of admission, but the liver function tests were abnormal (thymol turbidity 3; colloidal gold 2; thymol flocculation 1; hippuric acid excretion test, 0·3 g. sodium benzoate). The urine showed small but pathological amounts of coproporphyrin. The combination of jaundice, photo-

sensitive dermatosis and small amounts of coproporphyrin suggested that this might be a case of porphyria cutanea tarda.

Case 5.—A European female aged 30 years was admitted in October 1951. Her illness had started a month before admission during the post-operative period following hysterectomy, when she developed severe backache, pains in the limbs and constipation. A few days later she became mentally confused, disorientated and hallucinated. A slight brownish pigmentation of the face had been noted a few days before admission. Numerous drugs had been taken before and after the operation.

On examination there was a blotchy brown pigmentation of the face, and the patient was mentally confused. The urine contained uroporphyrin and coproporphyrin up to 12·7 mg. per day, but no porphobilinogen. She recovered from the mental symptoms within about three weeks and was discharged from hospital.

In November 1951 she was seen again as an out-patient with erythema and oedema of the hands following exposure to sunlight. There had been no recurrence of the mental symptoms; the pigmentation of the face was still present. One 24-hour specimen of urine at that time contained no porphyrin. This patient presented as acute porphyria, possibly toxic, with erythema and oedema which are very rarely seen in the acute form.

Comment.

In none of our cases was a family history of similar complaints obtained. It is worthy of note that four of our five cases were females; in the congenital type of porphyria males are said to predominate, the acute and tardive forms being far commoner in females.

Only one case had manifestations of porphyria apart from skin lesions, namely, Case 5, who was admitted in mental confusion. In her case, as in Case 3, the ingestion of drugs seemed to precipitate the symptoms of porphyria: they had both had recent hysterectomies. One patient, Case 4, had had a possible infective hepatitis shortly beforehand.

Four of the patients first had eruptions after exposure to sunlight, and two of them stated that mild trauma produced bullae.

In four of the cases the liver function tests revealed abnormalities, and in one of these there was clinical hepatomegaly. In any severe case of liver damage coproporphyrins may be found in the urine. In the present state of our knowledge the type of porphyrin excreted is of only slight diagnostic significance; however, porphobilinogen is characteristic of the acute type, although it appears occasionally in the tardive form; coproporphyrins I and III are the rule in the cutaneous tardive type; uroporphyrin I may appear in any of the types, but is found in large amounts in the congenital form. The role of the liver in the aetiology of porphyria is as yet uncertain, and its histology is not specific or helpful in solving the problem.

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CHRONIC FAMILIAL PORPHYRIA, WITH ASSOCIATED CHANGES IN LONG BONES.

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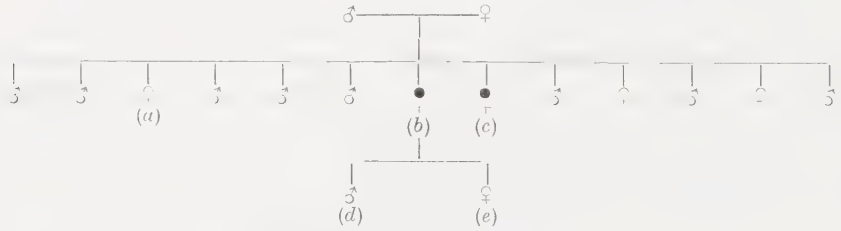
ALTHOUGH examples are rarely seen in any one hospital, enough reports of all types of porphyrinuria have been published to obviate the need for further reports that do not add to the general knowledge of the condition. The occurrence in two sisters of very similar lesions on the skin and peculiar radiological changes in the long bones is thought to be unusual enough to warrant publication.

CASE REPORTS.

CASE 1.—*Mrs. E. S—, aged* 25.

This patient is the seventh child in a family of thirteen, and the oldest living daughter. The eldest daughter (*a*) died at the age of eighteen months but the



cause is not known. Except for Mrs. M. R—, our second patient, (*c*) the other two sisters and the eight brothers are said to be unaffected. Mrs. E. S— (*b*) has had two children ; the first (*d*) died at the age of three days and no details are available ; the other (*e*) is now three years old and suffers from congenital deafness and a cleft palate. The Wassermann reaction has been repeatedly negative, and the child has never been found to have porphyrinuria. Neither of our patients is a very reliable witness, but consanguinity among the parents and grandparents is denied.

Mrs. E. S— was first seen by Dr. D. G. Freshwater on 29 September 1952, when she came to hospital complaining of infected blisters on the arms and legs. For as long as she can remember she has passed a bright pink urine, but gives no history of any other abnormality until the age of 22, when she started to get blisters on the arms, hands and shins. These blisters never appear above the elbow or knee, nor, according to the patient, have they ever been on the face. The blisters come mainly in the summer months and get bigger when they are rubbed : sunlight appears to have no connection with their onset, and the patient denies that they are started by

trauma. At no time has she suffered from any abdominal or neurological complaint that might be attributed to porphyrinaemia.

On examination.—The facial appearance (Fig. 1) is very striking, with dappled slate-coloured pigmentation on each temple and a very widespread lanugo hypertrichosis affecting most of the forehead and the face, which the patient shaves every week. All the teeth had been extracted at the age of sixteen but, as was found so often with these two patients, no reason could be given. On the lower part of the

Fig. 1.

legs (Fig. 2) and the backs of the hands were many oval or circular lesions. Most of these had been bullous and were secondarily infected, but there were several erythematous blotches from previous lesions. There was no scarring, and no milia were seen in the affected areas. The limbs were very hairy, but the sexual hair was normal and of female distribution.

Investigations.—The urine was bright pink and never changed colour. The report from the Biochemistry Department of Liverpool University stated, "large amounts of uroporphyrin (judging by ultraviolet fluorescence), and of coproporphyrin (absorption bands at 498, 529, 569, and 624 mμ in acetic acid-ether compared with

recorded figures of 495, 528·5, 568 and 623·5 m.μ). There were no other abnormal findings; the Wassermann reaction was negative and the blood-count normal."

Radiological findings.—Changes in the bone structure of the lower two-thirds of each femur were noted (Fig. 3). They were thinning of the cortex and accentuation of vertical trabeculation, giving an appearance of rarefaction to the extremities of

FIG. 2.

these bones. Various other bones were skiagraphed but no other bone change was noted.

CASE 2.—*Mrs. M. R—, aged* 24.

This patient was seen on 10 November 1952 at a different hospital complaining of ulcers on the hands and legs. These lesions appear during the summer months and she attributes them to heat rather than to sunlight or trauma. As did her sister, Mrs. M. R— denies ever having had lesions of the face. There are no complaints of neurological or abdominal abnormalities.

On examination.—The patient is strikingly similar to her sister, with hirsutes of the face and a slight melanotic dappling at the temples. All the teeth were removed some years ago because "they had gone bad." The arms and legs are very hairy, and there are oval lesions on the backs of the hands and the fronts of the shins with a slimy erythematous surface and a well-defined edge. An early blister arising from normal skin was seen on the back of the terminal phalanx of the left middle finger. Her urine also showed large quantities of uroporphyrin and coproporphyrin.

FIG. 3.

Radiological findings.—As in her sister, the bone changes were confined to the femurs, but this patient showed a more marked rarefaction.

DISCUSSION.

The lack of complete co-operation by these patients (no biopsies were permitted and further investigations were refused) makes an unsatisfactory record. They have chronic congenital porphyria and show the typical major skin changes—melanosis, hypertrichosis and blister formation. There is very little to suggest blistering on the face. Clinically, they seem to be very similar to the second case shown by Brunsting and Mason in 1947. The case

reported by Mackey and Garrod on several occasions (1922, 1926, 1936), which is mentioned later, was described as having features more closely allied to epidermolysis bullosa than to hydroa aestivale.

Bone changes are known to occur in porphyria, but usually consist of amputation or irregular erosion of the terminal phalanges of the hands. These

FIG. 4.—Normal femur for comparison with Fig. 3.

changes, however, are not specific and can occur in other conditions, such as scleroderma and psoriasis. In the same way the changes we have described above cannot be regarded as specific. It is, however, interesting that in the case reported by Mackey and Garrod there was atrophy of the terminal phalanges of the fingers, and in addition Dr. Brailsford commented on rarefaction of the extremities of the forearm bones. This appears to be the only reference to rarefaction of the long bones in this condition.

Summary.

Chronic congenital porphyria occurring in two sisters is reported.
Both have rarefaction of the lower end of the femur, a finding that does not seem
o have been recorded before.

Our thanks are due to Dr. D. G. Freshwater for allowing us to study his two cases, and to
r. G. D. Scarrow and Dr. P. Whittaker for their assistance with the radiological aspects. The
hotographs were taken by the University of Liverpool Central Photographic Department.

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SKIN DISEASE IN THE BRITISH ARMY IN S.E. ASIA III: THE RELATIONSHIP BETWEEN MYCOTIC INFECTIONS OF THE BODY AND OF THE FEET.

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In the first paper of this series (Sanderson and Sloper, 1953*a*) it was shown that tinea corporis was extremely common among British troops serving in Malaya and Hong Kong in 1947 and 1948. Mycological investigations (Sanderson and Sloper, 1953*b*) showed that out of 114 cases in which the infecting organism was recovered by culture, 94% were due either to *Trichophyton mentagrophytes* (Robin) Blanchard or to *Epidermophyton floccosum* (Hartz) Langeron and Milochevitch, or to both.

Many of the men also had lesions of the feet. This paper describes an attempt to determine what proportion of these lesions were due to fungi, and to assess the part played by mycotic lesions of the feet in maintaining the high rate of body ringworm.

It is widely held that tinea corporis usually arises as an extension of infection from the patient's feet, a supposition which requires careful consideration. It has been entertained since Djelaleddin-Moukhtar (1892) first described a simultaneous mycotic infection of the hands and feet. It was certainly held by Whitfield (1908), who identified mycelia in lesions of the feet and body of the same patient, and later by Sabouraud (1911), who recovered the causative organism from the affected sites. More recently, with the realization of the prevalence of tinea pedis, the theory has gained wide support. If it is true, one would expect to find as corollaries, first, that tinea pedis precedes and is commoner than tinea corporis; and second, that where the two conditions coexist they are due to the same organism. It is doubtful whether these corollaries are always true. Phillips (1944) found 2% of tinea corporis and 2·9% of tinea pedis among troops in England, but the latter figure is surprisingly low and without cultural observations is derived merely from the examination of scrapings for mycelia. Further, Phillips gives no indication of the relationship between the two conditions in individual cases. Jolly (1948), describing a military unit in which 22·5% of 400 men had tinea corporis, stated that

lmost all those with tinea corporis had tinea pedis, but did not quote the ncidence of the latter. The diagnosis of both conditions was made clinically, ave in two cases where mycelia were observed in scrapings from the feet. ther authors have described major outbreaks of tinea corporis due to *E. occosum* (Mercer and Farber, 1935) and to *T. mentagrophytes* (Pautrier and ietman, 1922) without taking any account of the feet.

Even if we accept that tinea pedis is the commoner of the two conditions nd that patients with tinea corporis usually have tinea pedis, it still does not llow that the two have a common aetiology. Thus, the commonest cause f tinea pedis in the U.S.A. and Germany in 1933 (Muskatblit, 1933 ; Schmidt, 933), and in England among troops in 1949 (Walker, 1950), was *Trichophyton nterdigitale*. Yet this dermatophyte rarely attacks the body. An even more ignificant point is that Hopkins and his colleagues (1947) recovered different rganisms from the body and feet in 34% of 115 cases.

Clearly it could not safely be assumed that in Malaya and Hong Kong the eet were the only or even the commonest source of infection of the body. ccordingly, an investigation was undertaken to determine :

(1) The identity of the organisms present in the feet.
(2) The proportion of cases in which the same organism could be recovered from the body and feet.
(3) The lesions of the feet most likely to act as a source of infection.
(4) The frequency with which cases exhibiting such lesions suffered from tinea corporis.
(5) The effect which measures aimed at suppressing infection of the feet might have on the incidence of tinea corporis.

Identity of the Organisms Present in the Feet.

The pathological methods employed have been described in the preceding paper (Sanderson and Sloper, 1953*b*). The subjects studied were British N.C.Os nd private soldiers in Singapore in 1947 and 1948.

96 hyphomycetes were recovered from the feet of 85 men, some presenting or examination during the investigation of tinea pedis, others during the investigation of the state of the feet of patients with tinea corporis. The results are hown in Table I. This survey is not a random one, but it is probably reasonably representative of the troops we were studying.

Table I.—*An Analysis of* 96 *Dermatophytes Recovered from the Feet of* 85 *European Soldiers.*

Number of cases.	Number of dermatophytes.	*T. mentagrophytes.*	*E. floccosum.*	*T. interdigitale.*	*T. rubrum.*
85	96	39 (40·6%)	43 (44·8%)	11 (11·5%)	3 (3·1%)

It will be seen that *T. mentagrophytes* and *E. floccosum* were each found in about half the cases studied. This seems to be the first outbreak in which *T. mentagrophytes* has been recovered from the feet with any frequency. The significance of the rarity of *T. interdigitale* in this series has been discussed in the preceding paper (Sanderson and Sloper, 1953*b*).

The Proportion of Cases in which the Same Organism could be Recovered from the Body and Feet.

In 49 cases an analysis was made of the organisms present on the body and the feet. The results are shown in Table II

TABLE II.

	Infections of the Feet.		*Infections of the Body.*		
			Different fungus recovered from body		
Variety of fungus recovered from feet.	Number of times in which fungus recovered from feet.	Number of times in which same fungus recovered from feet and body	*T. mentagrophytes.*	*E. floccosum.*	*T. rubrum*
E. floccosum	29	25	3	—	1
T. rubrum	2	1	0	1	—
T. interdigitale	2	1	0	1	0
T. mentagrophytes	19	19	—	0	0
Total	52	46	3	2	1

Only in six cases was the infection present on the body due to a different organism from that recovered from the feet. In short, in most instances infections of the body could have been derived from the feet.

The Lesions of the Feet most likely to Act as a Source of Infection.

It may be presumed that the most potent source of infection is the lesion where active growth and reproduction of the fungus is in progress. There is, however, a great deal of dispute concerning the diagnosis of tinea pedis. Dermatophytes have been recovered occasionally from normal toe-clefts (Williams, 1922; Kurotchkin and Chen, 1930; Peck, Botvinick and Schwartz, 1944; Walker, 1950); they have often been found in clefts whose clinical appearance could equally well be accounted for by physical factors, such as excessive sweating or abrasion due to vigorous towelling; and they have been isolated even more frequently from lesions typical of tinea pedis. It is only in this sense that tinea pedis is a clinical entity.

The clinical features of this condition thus require consideration. Peck and his co-workers (1944) regarded as " probably mycotic " those lesions with vesicles on soles or toes, fissures with vesicles in the toe-clefts, and fissures with scaling borders in the third and fourth toe-clefts. For " possibly mycotic "

lesions they required the presence of slight scaling, fissures in the toe-cleft, or maceration with varying degrees of hyperidrosis. Our own criteria, based on the findings in the clinical examination of the feet of 1424 men, are modified from those ; they reflect better the clinical types of lesions which we encountered in the tropics and which, incidentally, were due to different varieties of dermatophytes. We do not claim that our "probable mycoses" necessarily were tinea pedis, or that any appearances were characteristic of a single organism. Epstein (1938) observed lesions in the toe-cleft due to *T. mentagrophytes* identical with those due to *T. interdigitale* ; Hopkins and his colleagues (1947) were unwilling to distinguish between the lesions produced by *T. purpureum* (*T. rubrum*), *E. floccosum* and *T. gypseum* (probably *T. interdigitale*). We must also emphasize that we took no account of onychomycoses. This would constitute a serious omission, were it not that neither *T. mentagrophytes* nor *E. floccosum* commonly attack the nails. Nevertheless, it is possible that our series gives an unduly low figure for the recovery rate of dermatophytes from the feet, and that *T. rubrum* and *T. interdigitale*, both frequent causes of nail infection, were commoner than we have suggested.

A Classification of Lesions of the Feet.

(1) *Probable Mycosis.*

Lesions exhibiting either vesicles, or "broken vesicles," or a circinate outline—commonly all three.

(2) *Possible Mycosis* (*severe*).

Lesions exhibiting maceration, redness, and peeling but none of the characteristics of probable mycosis.

(3) *Possible Mycosis* (*slight*).

Lesions exhibiting either maceration, or redness, or peeling, or any two of these.

(4) *Normal.*

No lesion of any kind in toe-cleft or sole.

Probable mycotic lesions were commonly represented by circinate, red, peeling, often macerated, interdigital areas. Vesicles were often found, or else circular discontinuities of the epidermis, which were termed "broken vesicles." Other lesions were also seen, such as hyperkeratosis, denudation and fissuring ; they may be significant, but we did not use them in our classification. Minimal lesions, such as small areas of scaling and redness, were almost universal, and were probably overlooked in the initial examination of

the feet of 1424 men. Thus, in this initial survey 317 (22·2%) of these men were described as having normal feet : and yet, when normal feet were sought at a later date, it was only with the greatest difficulty that they were found.

The Detailed Investigation of 66 Men.

The feet of 66 men were the subject of a special investigation. These men came from various units stationed throughout Singapore Island. 385 scrapings were taken, both from normal skin and from lesions on the soles of the feet and toe-clefts. From 115 scrapings dermatophytes were recovered. Most of the men in this series were examined twice over a period of about a month. Some, however, were examined up to six times over a period of six months. Particular attention was therefore paid to the result of their first examination (Table III).

TABLE III.—*The Recovery Rate of Dermatophytes from the Feet of 66 Men at their First Examination.*

Description.	Number of cases.	Number from which fungi recovered.	Percentage recovery rate of fungi.
Normal	4	0	0
Possible mycotic (slight)	15	2	13·3
Possibly mycotic (severe)	5	2	40
Probably mycotic	42	32	76·2

It will be observed that the frequency with which fungi were recovered increased with the severity of the lesions. In particular, " probably mycotic " lesions yielded dermatophytes significantly more often than the rest.

Of the 36 cases from which fungi were isolated, 2 yielded both *T. mentagrophytes* and *E. floccosum*, 17 *E. floccosum* alone, 14 *T. mentagrophytes*, and 3 *T. interdigitale*. At subsequent examinations 9 men with " possible " lesions developed " probable " tinea pedis, bringing the number in this category up to 51. Dermatophytes were ultimately recovered from 44 (86·4%) of these.

These estimates of infection based on a single attempt to recover the fungus from the feet of suspected subjects are almost certainly too low.

In Table IV the same clinical classification has been used as in Table III, but applied to the individual lesions of toe-clefts and soles rather than to cases. The same conclusion emerges as from Table III : that is to say, under the conditions of the investigation it was easier to recover the dermatophyte from " possible mycoses " than from normal skin, and from " probable mycoses " than from " possible mycoses." It would, however, be difficult to show that the differences observed were significant, since the investigation was primarily concerned with demonstrating the frequency with which dermatophytes could be recovered from the feet. As a result, feet with lesions (and in particular with

TABLE IV.—*The Frequency with which Dermatophytes were Recovered from Individual Lesions and Areas of Normal Skin.*

Description of lesion.	Number of sites from which cultures made.	Number of sites from which fungi obtained.	Percentage of sites from which fungi obtained.
I. *Toe-clefts :*			
(i) Normal	43	4	9·3
(ii) Possibly mycotic (slight)	81	18	22·3
(iii) Possibly mycotic (severe)	31	7	
(iv) Probably mycotic	101	57	56·5
Total	256	86	33·6
II. *Soles :*			
(i) Normal	44	2	4·5
(ii) Possibly mycotic	57	9	15·8
(iii) Probably mycotic	28	18	64·3
Total	129	29	22·4

" probable mycoses ") were repeatedly cultured and thus received a disproportionate amount of attention.

The analysis of lesions rather than individual cases introduced yet another complication. It was necessary to take into account the possibility of the passive transference of the dermatophyte from an active infection to other parts of the skin. The suggestion that this could occur was originally put forward by Schramek (1917), who described the presence of mycelia on the normal skin adjacent to interdigital infections. If analogy with bacterial lesions is any guide a passive transference of this kind is not uncommon. In the present series, provided it was assumed that all " probable " lesions were mycotic, this mechanism could have accounted for every instance in which dermatophytes were recovered from normal skin, and for all but four instances in which dermatophytes were recovered from " possible " mycoses of the feet. It may be that in the remaining four cases the presence of the dermatophyte was not fortuitous, and that these " possible " mycoses may at times have been subclinical infections. There was, however, no means of determining the incidence of such infections. We do not therefore claim either that passive transference always occurred, or that all " probable " lesions were mycotic. We merely conclude first, that these " probable " lesions were more likely to have been mycotic than any others; and second, that feet so infected constituted an important reservoir of infection.

The circinate " probable " mycoses occasionally spread to the dorsum of the foot and from the sole to the instep, and in such cases their mycotic aetiology could not be doubted. Many lesions, however, especially in the " possibly mycotic " group, yielded no pathogenic fungi on culture, and it seemed possible that some other agent might be responsible. In a search for other possible causes we subcultured all yeast-like colonies found on the primary beer-wort-

agar culture on to maltose peptone agar, and then studied their sugar fermentation reactions. *Candida albicans* was identified in this way in only two sites, both of which also yielded pathogenic fungi. However, pyogenic cocci were probably frequently present. In one small series of 21 cases Captain J. R. May took cultures from sites which we scraped for fungi. The organisms recovered from 72 sites on the feet of these men is recorded in Table V.

TABLE V.—*The Frequency with which Dermatophytes and Pyogenic Cocci were Recovered from Individual Sites.*

Sites from which cultures made.	Number of sites.	No pathogen recovered.	Pathogenic hyphomycete.	Pathogenic yeast.	B-haemolytic streptococcus and/or coagulase + staphylococcus.
Normal soles and clefts	18	15	0	0	3
Possibly mycotic	40	23	9	0	12
Probably mycotic	14	4	7	1	5

It should be noted, first, that these cocci were far easier to isolate than the slowly growing dermatophyte ; and second, that in none of the sites cultured was there any evidence of an acute bacterial inflammation. Consequently, in spite of the frequent recovery of potentially pathogenic bacteria from these sites, it is likely that a proportion at least of " probable mycoses " were tinea pedis. These were clearly the most likely sources of infection for tinea corporis.

The Frequency with which Men Exhibiting Foot Lesions Suffered from Tinea corporis.

The next step lay in determining the extent to which the carriage of dermatophytes by the feet predisposed the person to tinea corporis. That such a predisposition existed was likely in view of the frequency with which organisms were recovered from the feet ; 44 of the 66 men investigated as described above ultimately yielded fungi from the feet, while 32 of the 66 developed tinea corporis. None of the four men with normal feet were so affected.

A rough estimate of the incidence of tinea pedis compared with that of tinea corporis in a larger body of men was obtained by examining two infantry companies ; the results are shown in Table VI.

TABLE VI.—*The Clinical Examination of* 141 *Men.*

Number examined.	Normal feet.	Possibly mycotic (slight).	Possibly mycotic (severe).	Probably mycotic.	Body ringworm.
141	0	41 (29·1%)	16 (11·3%)	84 (59·6%)	39 (27·7%)

All the men showed some clinical abnormality of the feet, and from our previous experience of the relationship between the recovery rate of fungus and clinical category it can be inferred that dermatophytes would have been recovered from about 50%. Thus the incidence of fungal infection of the feet was almost certainly higher than that of body ringworm.

Nevertheless, it must be admitted that those with "probable mycoses" of the feet were very little more affected by tinea corporis than those with "possible mycoses," for 27·6% of the former and 26·1% of the latter had tinea corporis. Probably in this group of men other sources of infection than the feet were also responsible for tinea corporis.

The Effect of the Suppression of Tinea Pedis on the Incidence of Tinea Corporis.

An experiment intended to demonstrate the importance of tinea pedis as a source of tinea corporis has been described by Jolly (1948). This observer, studying an outbreak of tinea corporis among British troops in Java, introduced measures designed to reduce the incidence of tinea pedis and to prevent spread of infection from feet to body. He attributed the fall in incidence of body ringworm which ensued (from 22·5% to 2·5%) to these measures; but he introduced at the same time frequent skin inspections and efficient regular treatment, and it is not clear from his results that the latter was not the cause of the improvement. In the experiment to be described an attempt was made to separate the effects of efficient treatment from those of prophylaxis.

A stationary unit was selected and arrangements made for all cases of body ringworm to be treated by one of the authors. At the same time weekly skin inspections by the same observer were begun. The treatment used at the outset was daily application of 2% chrysarobin in Lassar's paste to the body lesions, preliminary therapeutic trials having shown this to be one of the most effective agents available. Later, increasing strengths of chrysarobin, up to 6%, and more frequent applications, up to three times daily, were used, with some reduction in the number of resistant cases. The progress of this part of the experiment is shown in Table VII.

Table VII.

Week of experiment.	Number of men.	Total cases.	%
1	480	111	23·1
2	467	84	18·0
3	467	71	15·2
4	473	70	14·8
5	464	71	15·3
6	425	77	18·1
7	381	63	16·5
8	398	62	15·6
9	360	61	17·0
10	367	56	15·3
11	357	67	18·8

It will be seen that after an initial fall in the first week the rate fluctuated between about 15 and 18%—an improvement on the original state of the unit, but by no means satisfactory. It may also be noted that the reduction in incidence is very much smaller than that obtained by Jolly in his experiment.

At this point an attempt was made to prevent the occurence of foot-to-body infection in part of the unit. The method chosen was to issue to the barrack-rooms of the men selected the following foot-paint :

Salicylic acid . . .	20 parts
Benzoic acid . .	40 parts
Brilliant green . . .	1 part
Spirit to	1000 parts

All the men in these barrack rooms were told to apply this paint to their toe-clefts and flexures every morning and evening regardless of the state of their feet. The brilliant green served as a marker, to show whether the paint was being used properly ; the intensity of the staining was found to fade rapidly in 24 hours, and defaulters in the use of the paint were readily detected. The average strength of the "protected" group (Group F) was 146. The rest of the men in the camp were used as a control group (Group G) ; their average strength was 200.

The subsequent course of the experiment is shown in Table VIII.

TABLE VIII.—*Incidence of Body Ringworm* (%).

Week of experiment.	Group F (protected).	Group G (control).
11	17·8	19·5
12	17·8	16·4
13	12·4	13·4
14	13·0	11·8
15	11·0	13·3
16	8·9	13·0
17	—	—
18	5·5	12
19	5·5	10
20	4·1	12
21	6·2	9·5

The course of the whole experiment is depicted in graphical form in Fig. 1. It will be seen that immediately following the introduction of the use of foot paint in Group F, there was a fall in the incidence in both groups, lasting for some three weeks : the cause of this fall is not clear. After week 14 the figures for the two groups began to diverge, that for Group F falling to 4–6% while Group G remained at 9–12%. This fall in the incidence on Group F is attributed to the use of the foot paint.

The influence of the foot paint is shown even more strikingly by the figures for new cases of body ringworm in the two groups. In preparing these figures

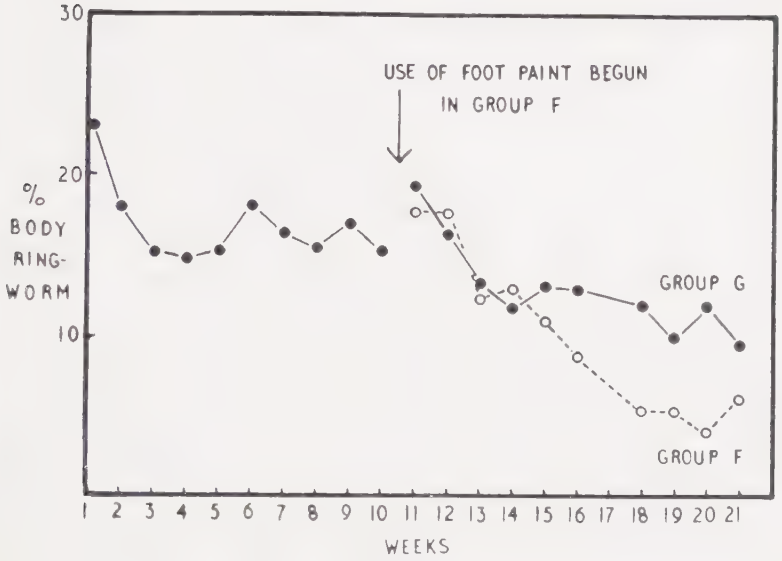

Fig. 1.

relapses at sites known to have been infected previously with ringworm have been excluded: only new cases and old cases infected at sites not previously involved were counted. On this basis the new cases occurring during the ten full weeks when the foot paint was in use were as follows:

Group.	New cases.	% new cases.
F (146 men)	8	5·5
G (200 men)	29	14·5

Seven new cases which would otherwise have been included in Group G were excluded because they had been in the camp less than two weeks and might therefore have become infected in their previous unit, where the general tinea rate would probably be higher: they would thus be unsatisfactory controls. The above figures examined by the χ^2 test, are seen to be highly significant ($\chi^2 = 6{\cdot}27$; $P = 0{\cdot}02$).

Our data therefore provide additional support for Jolly's conclusion—namely, that measures aimed at suppressing tinea pedis cause a fall in the incidence of tinea corporis.

Discussion.

These results are consistent with the widely-held belief that body ringworm is commonly acquired as an extension of a pre-existing fungus infection of the feet: they provide perhaps somewhat firmer evidence than is commonly adduced. It is unlikely, however, that this is the only source of body ringworm. In some units, as has been noted above, body ringworm rates of over 50% were

found, and in such circumstances it is possible that body-to-body spread occurred. However, the importance of the feet as a reservoir of infection seems clear. It follows from this that in any extensive outbreak of tinea corporis some degree of control may be expected from measures aimed at reducing the incidence or the infectivity of tinea pedis. The complete eradication of tinea pedis under the conditions of Army life in the tropics is impracticable and probably unnecessary, since it is not usually in itself a disabling disease. Measures designed to prevent its spread both to the subject's own body and to the feet of his fellows would seem to offer the best prospect of avoiding widespread tinea corporis.

Summary.

1. The existing evidence for the supposition that tinea corporis is usually acquired from tinea pedis is examined.

2. Data obtained from British troops in the Far East are presented to show that—
   (i) where tinea corporis and tinea pedis coexisted they were usually due to the same organism ;
   (ii) tinea pedis was commoner than tinea corporis ;
   (iii) measures aimed at suppressing tinea pedis reduced the incidence of tinea corporis.

3. It is concluded that in the population studied, tinea corporis was often acquired from the patients' own feet.

4. The relationship between clinical appearances and recovery-rate of pathogenic fungi in foot lesions studied is described.

Our thanks are due to Professor J. R. Squire and Dr. J. T. Duncan for help at all stages of the investigation ; to Professor G. W. Pickering and Dr. H. B. May for help with the manuscript ; to the technicians of the Dermatological Research Team, R.A.M.C., for their technical assistance ; and to the Director-General, Army Medical Services, for permission to publish this paper.

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ROYAL SOCIETY OF MEDICINE.

SECTION OF DERMATOLOGY.

President—Dr. G. B. Dowling.

15 January 1953.

Sclerema Neonatorum.—Dr. R. T. Brain.

The patient, H. S—, was a female infant aged 5 weeks when brought to hospital. She had been a full-term baby delivered after a normal labour lasting about seven hours and the birth-weight was 8 lb. The mother's pregnancy had been uncomplicated, and it was unlikely that she had had any dietary deficiencies. About the third or fourth day of the infant's life an extensive dusky bluish area was noticed on the back, extending from the lower rib margins to the base of the neck and in the lower part of this area two large swellings were observed (Fig. 1). The infant was breast-fed and her general condition and nutrition were good.

Fig. 1.—H. S—, aged 6 weeks, showing two cystic swellings.

Examination.—The infant was sturdy and healthy, and the only abnormal feature was that the skin across the back and shoulders was brownish-red with an irregular nodular surface, here and there causing coarse creases near the edges. In the lower part on each side of the mid-line were two soft fluctuating communicating cysts 3-4 cm. in diameter. When the centres of these soft swellings were depressed with the fingers, a firm collar of indurated subcutaneous tissue was felt to surround the base of each. This induration was continuous over the affected area and resembled a waxen plaque approaching 1 cm. in thickness. It was possible to insert the finger-tips beneath the well-defined edges, especially near the neck, and it seemed that the

induration involved the hypoderm. The skin was firmly attached to it but was otherwise relatively normal in texture.

On aspirating the cyst a thick creamy sterile fluid was obtained containing no cells but only fat droplets and doubly refractile crystals.

Skiagrams of soft tissues showed no calcification.

Histology.—The fat excised from the affected area was hard, opaque, white and avascular. Sections (Dr. M. Bodian): "The cutis shows only minimal changes, slight oedema and very little cellular infiltration. There is some variation in the size of fat cells, which have, on the whole, preserved their outline. Needle-like crystals lie in the fat (and some outside) mostly in radiating tufts and some singly. Whenever they lie outside the cells they are colourless, but within the fat cells they appear to take up the stain for neutral fat; this, however, is probably spurious. A granulomatous infiltrate in the fibrous septa around the fat lobules spreads also into the lobules. This consists of histiocytes, lymphocytes and polymorphonuclear leucocytes, but foreign body giant cells are also present in apposition to some of the fat cells."

Comment.—I reported a very similar case in 1947 without cystic lesions that resolved almost completely in two months.

The special interest of this case is in the two fluctuant swellings. Such swellings are distinctly rare, although Sir Archibald Gray's (1926) first two patients showed them. They may be mistaken for abscesses or cavernous haemangiomata.

No notable contribution has been made since the work of Channon and Harrison (1926) on the chemistry of the fat. The conclusion was that a relative deficiency of olein with a preponderance of stearin and palmitin gave a high melting-point to the body fat and that, possibly, cooling of the skin led to the deposition of needle-like crystals which provoked a foreign-body granulomatous reaction. Although the investigations of Harrison led to the inference that the crystals were natural fat, neither the evidence nor the explanation was entirely satisfactory, since in view of the fact that an infant's fat contains less olein than that of an adult, it is surprising that sclerema neonatorum occurs so rarely and is not much more common in cold climates.

The differential diagnosis involves the separation of this entity from oedema neonatorum, scleroderma, pre-agonic or cadaveric induration of the fat of the newly born and possibly from what is described as subcutaneous fat necrosis of the newly born. One would expect subcutaneous fat necrosis to be localized and usually traumatic but, whether traumatic or idiopathic, saponification of the necrotic fat tissue would result in the early formation of free fatty acids and deposition of calcium salts. Harrison was unable to find free fatty acids in his investigations of material from sclerema neonatorum. Pre-agonic or cadaveric induration is so obviously an ante-mortem solidification of the fat in a marasmic, moribund infant that it could scarcely be confused with sclerema neonatorum, except in the rare case when the latter disease involves the trunk and limbs, with in consequence, a serious prognosis.

I am indebted to Dr. C. H. Whittle and to Dr. O. P. Bewers, the attending practitioner, for this interesting patient, and to Mr. D. Martin for the excellent photograph.

[After showing a photograph of his case, Dr. Brain showed a second photograph illustrating the patient he saw with Dr. E. Davis in 1945. The clinical condition was very similar to that of the patient shown to the meeting but no cysts were present (see Davis and Brain, 1947).]

Postscript (June, 1953).—Progress: The clinical condition had resolved in two months.

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Urticaria Pigmentosa with Bone Lesions. Two Cases.—Dr. C. D. Calnan.

(1) K. P—, female, aged 24.

History.—Three years ago: Onset of eruption on legs and arms, and some lesions scattered on trunk. They become red and wheal with friction or heat.

Examination.—The arms, legs and chest show urticaria pigmentosa of the adult type.

Investigations.—Biopsy: Numerous mast cells in the dermis, especially around blood vessels. Skiagram of skull: There is an annular clear-cut deficiency about 1 cm. diameter of both tables in the L. parieto-frontal region in the line of a suture. The margins are sclerosed (Fig. 1).

(2) E. F—, female, aged 52.

History.—Five years: Rapid onset of the present eruption which itches at times, especially when the skin is exposed to a fire or hot water. It is present on the arms, legs, and more sparsely on the trunk.

Examination.—Lesions of urticaria pigmentosa of adult type on the forearms, arms and lower legs, and a few on the trunk.

Investigations.—Skiagram of skull: There is a small ill-defined defect in the right frontal bone about 5 mm. diameter (Fig. 2).

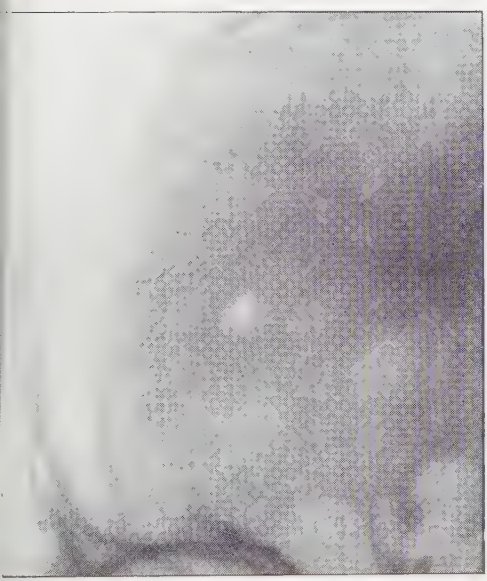

Fig. 1.

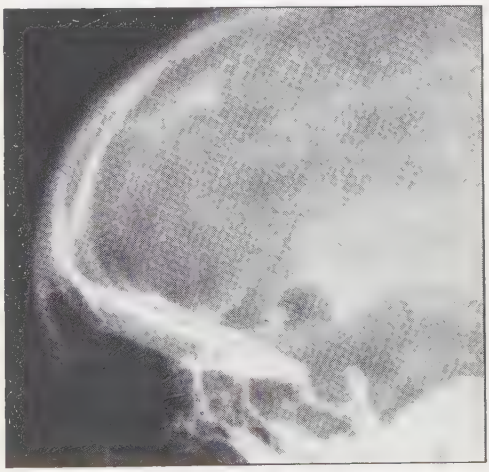

Fig. 2.

Comment.—These cases are presented in order to discuss the significance of bone lesions in urticaria pigmentosa.

I became interested after reading of Felix Sagher's patient who had cystic osteoporosis of the ribs and vertebrae (Sagher *et al.*, 1952). (Clyman and Rein, 1952, also have examined about 6 patients.) There is no specific diagnostic feature about the skiagrams of my patients, and the abnormalities could well be due to other incidental pathological processes. There is, however, some evidence for regarding this condition as a systemic disorder, and French authors not infrequently classify their cases as mast-cell reticulosis (Hissard *et al.*, 1951).

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Sarcoid after Injury.—Dr. R. G. Howell (for Dr. G. B. Dowling).

M. F—, male, aged 32.

This man was blown up by a booby-trap in Palestine in 1945. His face and shoulders were peppered with soil particles. When seen in 1951 there were many small brown-red papules scattered among the black pigmented marks of his injuries. He could not say when the nodules first appeared, and they have remained unchanged since 1951. The spleen was not palpable and there were no enlarged lymph glands. The general health was good.

Investigations.—Skiagram of chest and hands revealed no abnormality. Mantoux 1/1000 negative.

Histology of a nodule from the shoulder (Dr. Ian Whimster).—The dermis contains numerous discrete and confluent tubercles. Doubly refractile, colourless, crystalline foreign bodies are present in the tubercles, sometimes inside giant cells, but are also present in the dermis where they do not appear to be exciting any inflammatory reaction.

Treatment.—Foreign bodies have been removed from both eyes and a right corneal graft done. No treatment has been given for the skin lesions.

Comment.—Silica particles in the skin may excite a particular tuberculoid local inflammatory response, or if the patient develops sarcoidosis subsequent to the injury, the silica particles may preselect the site of the lesions.

In R. D. Sweet's case, sarcoid tissue was found in lymph glands quite independent of silica deposits. Silica particles in the skin are only rarely associated with "sarcoid" tissue. It appears then that they may preselect the sites of development of lesions in a generalized disease.

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Scleroderma.—Dr. C. H. Whittle and Dr. J. Moffatt.

Mr. A. B—, aged 53; telephone operator.

This patient came with a gradually extending eruption of 3 years' duration. The lesion began on one side of the lower abdomen and remained about 1 in. to 2 in. in diameter for almost a year but then spread to the other side. In the last year it has spread considerably. The lesions have never caused anything more than slight irritation, and there has never been any exudation.

On examination he has:

(1) Large plaques of either side of the abdomen. They are pigmented with some telangiestasia and a pinkish edge fading gradually into the normal skin. The edge is just palpable, and the skin feels slightly thicker than normal. Small white areas are developing in the middle of these lesions, particularly on the right.

(2) Below each shoulder blade is an area of slight erythema, about 3 in. to 4 in. in diameter. The skin in these areas is finely wrinkled. There are similar, less obvious lesions in the axillary line on either side of the chest.

(3) There is pigmentation and telangiectasia of the skin overlying the lower thoracic and lumbar spine.

(4) There is pigmentation on both feet and telangiestasia below the internal malleoli.

There does not appear to be any other sign of scleroderma, and there is little of note in his previous history.

Investigations.—Histological section : This shows some degree of atrophy of the epidermis, slight perivascular cellular infiltration and homogenization of the papillary layer of the corium, and increased density of the deeper part of the corium.

Blood count and E.S.R.—Within normal limits.

Urinary creatine and creatinine.—2·1 g. per day.

Wassermann and Kahn reactions.—Negative.

Granuloma of Face. For Diagnosis.—Dr. G. A. Beck and Dr. C. H. Whittle.

Mrs. C. McC—, aged 33.

She was seen on 12 November 1952 with a painful red roughly circular lesion 4 cm. in diameter in the left preauricular region.

She often has " blind " boils on her chin that come up as small red papules and gradually subside after 2 or 3 weeks. The present lesion started similarly, but after remaining as a papule for 3 weeks it started to spread and became painful about 3 weeks before coming to hospital. There were scattered yellowish nodules, principally at the edge, which looked like pustules but from which only a little serum could be obtained.

A provisional diagnosis of kerion was made and the lesion treated with hot compresses of perchloride of mercury. It has continued to enlarge and has developed a slightly scolloped margin, which in places shows a dull yellowish cord-like border. The lesion is plum coloured and raised 3 mm. above the surface in its outer part, tending to heal at the centre. It is 7 cm. in diameter. There is some scaling and no discharge.

Past history.—Aged 13, tonsillectomy for repeated sore throats. Aged 21, total extraction of teeth. Aged 23, red weeping eruption of her feet for 4 months. 6 months ago felt out of sorts and was treated with an " iron tonic " and halibut liver oil.

Investigations.—General physical examination : N.A.D.

Skiagram of chest : Normal.

Blood count : Hb. 14·3 g./100 ml. Normochromia, normocytosis.

W.B.C. : 11,000/cu. mm. Neutrophils 82%, eosinophils 1%, basophils 1%, lymphocytes 8·5%, monocytes 7·5%.

E.S.R. (Westergren, corrected) : 9 mm. in 1 hr.

Wassermann : negative.

Swab from lesion : A few colonies of micrococci. No fungus grown.

Histology (15 December 1952) (Dr. A. M. Barrett).—No organisms in Gram preparation. No fungus elements in periodic acid Schiff and toluidine blue preparations.

Intense reaction extending deep into corium, tends to be perivascular and tends to spare papillary layer and around appendages. Reaction is inflammatory with areas of granulation tissue infiltrated by eosinophils and neutrophils, and others, frankly purulent, with predominantly neutrophil leucocytes. Occasional leucocytes in epidermis.

We should like your views as to whether kerion can go on as long as this without breaking down, and if not, what members think the granuloma is.

Dr. R. E. Bowers : I have had a very similar case to this lasting three to four months. *Trichophyton discoides* was grown on culture.

Dr. L. Forman : Occasionally a kerion will not respond to external applications. I have seen an extensive and intractable kerion of the neck clear up with intravenous iodine.

Dr. Whittle : Does Dr. Forman think it is a kerion ? We have no evidence ; the cultures were negative.

Dr. Forman : I thought it was.

Dr. P. J. Hare : Would it be worth while trying a trichophytin test ? If the lesion is a kerion a strongly positive reaction would be expected.

Dr. H. J. Wallace : Is there any possibility of this being a halogen reaction ? She told me that she had been taking medicine from her doctor for many weeks.

Dr. R. T. Brain: It can be difficult to discover the fungus in these cases. X-rays in doses of 200 r may help; various fungicides in a penetrating base can be tried, with occasional painting with liquid phenol.

Dr. G. A. Beck: The lesion was treated with hot compresses of perchloride of mercury lotion, which caused considerable local reaction and no benefit. It was still increasing in size when she was last able to visit us a fortnight ago, but has since improved to its present condition with a suggestion of healing at the centre.

She had has no systemic treatment from us. Her doctor gave her an "iron tonic" for three weeks last summer. She has taken no other drugs including iodides.

Postscript. (5.iii.53).—The lesion has enlarged slowly but steadily and now encroaches on the eyelids. Cultures for fungus in the crusts have again been negative.

(18.vi.53).—The granuloma has now completely healed.

Case for Diagnosis. ? Granulomatous Mycosis. ? Squamous Carcinoma.—Dr. Brian F. Russell.

H. W—, aged 81.

History.—In December 1951 the patient, a keen gardener, abraded the knuckles of his right hand. A swelling developed and slowly spread over the back of the hand with ulceration and scarring behind the spreading edge.

On examination. (5 December 1952)—On the back of the right hand there was an area approximately 5 in. by 5 in. with irregular central scarring and a firm, raised, skin-coloured edge from the inner side of which cheesy pus exuded from several pockets. There were many follicular plugs and several epidermal bridges. The epitrochlear and axillary lymph nodes were not palpable.

At a subsequent examination a dusky fluctuant nodule was present on the right thenar eminence from which thin, blood-stained fluid was aspirated. The other sinuses had become dry.

Histological section showed a well-differentiated squamous cell epithelioma.

Tissue from hand.—Film: No pus cells. Very many Gram-negative bacilli and Gram-positive cocci.

Culture: Profuse growth of an anaerobic Gram-negative bacillus, probably *Fusiformis fragilis*; sensitive to aureomycin and terramycin; slightly sensitive to streptomycin; insensitive to chloromycetin. *Staphylococcus saprophyticus.* No fungi isolated.

Blood count.—Haemoglobin 97% (14.3 g. %), Leucocytes 10,500, polymorphs 74%, eosinophils 2%, lymphocytes 19%, monocytes 5%, red cells and platelets normal.

Blood Wassermann reaction.—Negative.

Comment.—I think the diagnosis of squamous epithelioma is wrong and that this is an example of pseudo-epitheliomatous hyperplasia. A similar condition in an old man has resisted all the efforts of myself and others for about 20 years. So far, repeated searches for fungus have been negative, from which it seems that this must be a bacterial or virus infection. The condition resembles or may even be identical with acne conglobata from an extensive case of which recently under my care a pure growth of diphtheroids was obtained.

I think that the anaerobic organisms found in this case may be responsible for the condition, but as they are situated in the depths of the lesions it is difficult to dispose of them adequately.

Dr. Daphne Anderson: I would like to say a few words about this case because of the one that was shown here in October 1952 (Anderson, D. S., and Seville, R.). It was clinically a pseudo-epithelioma of Azua, but histologically it showed frank squamous-celled carcinoma in one area. Since 1894, when Azua first described "pseudo-epithelioma" there has been a group of conditions similar to this, localized vegetating pyodermias with very long histories. Clinically they have certain features in common. There are raised lesions which may or may not have everted edges. They usually have this peculiar follicular plugging; when much raised they are like a sponge—if pressed, both pus and keratin plugs are extruded. Histologically they may show pseudo-epitheliomatous downgrowth or all gradations to squamous-cell carcinoma. There have been recorded in 1951, by Gay Prieto and Cascas, a number of cases seen in Spain, where it is not uncommon.

The case we had was radio-resistant.

Reference.

Gay Prieto, J., and Cascas, M. A. (1951) *Dermatologica*, **103**, 135.

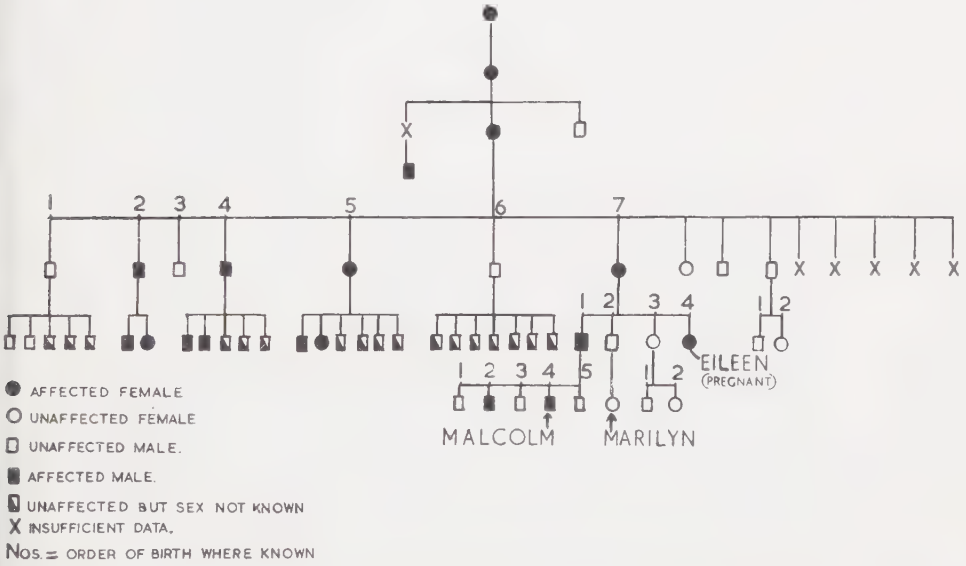
Epidermolysis Bullosa Dystrophica.—Dr. P. J. Feeny.

A boy, aged 6.

Since birth slight trauma has produced bullae, especially over the knees, elbows and ankles. The bullae are followed by crusting, pigmentation and slight atrophy but they are never haemorrhagic. There are never any buccal lesions. Well-marked nail dystrophy is seen. No porphyrins were present in those specimens of urine examined. On section the bullae are seen to be subcorneal.

Family history.—18 members of 6 generations known to be affected (see diagram). No buccal lesions. No haemorrhagic bullae. Lesions mainly confined to the skin of the knees and elbows. Marked atrophy of the affected skin of the knees and elbows seen in Malcolm's paternal grandmother. No tardive cases.

Family tree shows non-sex-linked dominant inheritance. Thought to have originated 120 to 130 years ago.



All are heterozygotes. Half of Eileen's children are likely to be affected. Marilyn was born in hospital during this investigation. No porphyrins were present in those specimens of her urine examined.

Dr. E. J. Moynahan: I have seen a similar case in a family with a similar record. It shows the features brought out on the family tree. If it skips a generation it does not appear again. I have seen that in several family trees of epidermolysis bullosa even of the simplest variety; if one descendant does not show the trait none of his descendants will, and similarly if it is present in one descendant then her descendants, roughly in the proportion shown, will exhibit it. I have one family tree, covering not quite a hundred, going back about six generations.

Dr. D. S. Wilkinson: I have a family with a number of members having a very mild type of epidermolysis bullosa on the feet, as Cockayne described. They all breed true to type and there are no severe or dystrophic cases. It seems as if there might be a complex or multiple genetic background, with only one gene being abnormal in some families.

Hypertrophic Lichen Planus with Epitheliomata.—Dr. Harold Wilson.

Mrs. H. D—, housewife, aged 77; widow.

This patient first attended hospital in 1936 for several small ulcers of the legs which were thought to be unusual varicose ulcers. They were associated with an itching red scaling eruption on the limbs which did not respond to out-patient treatment. In 1938 when she was taken into hospital it was noticed that there were also

several small bluish papules on the elbows, forearms and thighs, which were thought to be early lichen planus lesions. She has attended hospital intermittently since and has been treated with occlusive dressings, bismuth injections, mercury by mouth, and in 1941 liquor arsenicalis minims 5 *t.d.s.* for one month. Since then the rash has cleared from the arms but has remained as indolent hypertrophic patches forming a slightly reticulate pattern on the legs.

In August 1949 a patch on the left calf became thickened to form a tumour which was found on histological examination to be a squamous-celled carcinoma (Fig. 1). No amyloid was found. This was treated with surface radium, 6000 r being given over eleven days. Six months later a second epithelioma appeared above the original one. This was treated with x-rays 6000 r at 120 kv. and 3 m.a. An ulcer developed

FIG. 1.

at the site of the first epithelioma and did not heal for twelve months ; the second lesion healed satisfactorily. There has been no recurrence.

She is obese, with osteoarthritis of the knees. Blood pressure 210/100. Pulse irregular from extrasystoles. General condition otherwise good.

Epithelioma does not commonly complicate lichen planus. Lyell and Whittle* showed a case here in 1951, and the French literature contains records of twelve cases of lichen planus of the mucous membrane which became malignant. In this case I wondered if the patient had been given arsenic in the past, and found that in 1941 she had been treated with liquor arsenicalis minims 5 *t.d.s.* for a month, a total of 4 grains of arsenic in all.

It is possible that the epitheliomata developed as a late result of the arsenic given 15 years or so before.

* Lyell, A., and Whittle, C. H. (1951) *Brit. J. Derm.*, **63**, 69.

The following cases also were shown :

Congenital Ichthyosiform Erythrodermia (Brocq) with Bullae.—Dr. R. G. HOWELL (for Dr. H. J. WALLACE).

Partial Congenital Ichthyosis.—Dr. R. G. HOWELL (for Dr. H. J. WALLACE).

OXFORD REGIONAL DERMATOLOGICAL GROUP.

24 January 1953.

? Giant Granuloma Annulare.—Dr. Alice Carleton.

A woman aged 59.

History.—General health good save for indigestion relieved by a low fat diet. In April 1951 she began to develop on the arms and the upper part of the trunk solid pale pink elevations, which flattened in the centre and spread in annular fashion. There are no subjective symptoms.

On examination. Some large antecubital lesions are disappearing, but small fresh elevations are visible on the sides of the neck. The periphery of the ring is a solid cord-like elevation, pale on the outside and lilac on the inner slope. It is never vesicular or scaly. The centre of the patch is slightly discoloured and in some lesions atrophic, so that if the skin is pinched up it remains so for a few seconds. These rings take about three weeks to develop, remain stationary for months and undergo partial involution as others appear. They range from 1 to 18 cm. in diameter. Heart, chest, central nervous system, abdomen normal. She is obese.

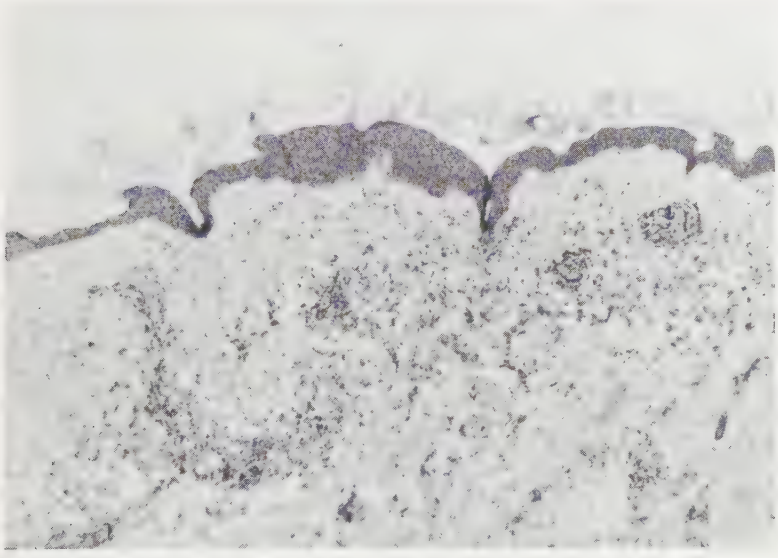


Fig. 1.

Investigations.—Haemoglobin 95%. W.B.C. 6000. E.S.R. 18 mm. in 1 hour (Westergren). Blood cholesterol 199 mg.%. Fasting blood sugar 101 mg.%. Plasma protein total 5·6 g.%; albumen 3·1 g.%. Wassermann and Kahn reactions negative. Blood pressure 140/90. Mantoux 1 : 1000 positive.

Skiagrams: Chest normal; cholecystogram normal; hands, slight arthritic lesions in interphalangeal joints.

Histology (Dr. Robb-Smith).—The striking lesion is present in the dermis, and consists of foci of giant cells of small foreign-body type, scattered among the collagen

fibres of the deeper layers. The collagen about these cell-aggregates is fragmented and appears to be undergoing necrobiosis. This process is at its height in the thickened edge of the lesion ; in the central scarred area giant cells are fewer and are scattered sparsely in the subepidermal zone, not in the deeper layers. Apart from the very striking giant cell infiltration, there is well marked perivascular cuffing in the superficial dermis, in both the thickened and the central area ; this is almost exclusively lymphocytic. Elastic fibres are somewhat reduced in number in the thickened area, coarsened and fragmented, while in the central area they are absent in the lower dermis, as if scarring had occurred there. Clumps of orcein-positive material are not infrequently found in the cytoplasm of the giant cells (Fig. 1).

The lesion is essentially a necrobiosis of the collagen, spreading centrifugally and leaving a scarred and somewhat thinned dermis centrally. This type of picture inevitably suggests a lesion of the granuloma annulare-necrobiosis lipoidica type. Sections stained for metachromasia are negative ; unfortunately tissue has not been preserved for a fat stain, so that the histological diagnosis, by exclusion, of necrobiosis lipoidica, is only presumptive.

Discussion.—Clinically, this case seemed more like erythema annulare centrifugum than anything else. The continuous unbroken ring without nodules, scales or vesicles is as described by Darier. Furthermore, the size of the larger patches is unusual in granuloma annulare. However, the histology rules out the diagnosis of erythema annulare centrifugum.

Fixed Drug Eruption.—Dr. Alice Carleton.

A girl aged 9.

History.—Two years ago this child began to develop round, scaly, slightly vesicular spots which were diagnosed by her doctor as tinea. In about three days the scales disappeared and the areas became deeply pigmented. Lesions are present on the trunk, the upper arms and thighs. One spot includes the right nipple.

On examination.—The spots are mostly circular though the larger ones are a little irregular in shape. The coloration, originally dark sepia, is paling to *café-au-lait*, and the macule at the root of the neck is showing signs of disappearance. The child is of brunette colouring and otherwise healthy.

Histology.—The epidermis shows very slight hyperkeratosis. There is no appreciable overactivity of the melanoblasts in the basal layer. Very numerous melanophores containing densely packed melanin granules lie in the dermis, forming an almost complete line a short distance from the epidermis. Scattered lymphocytes and plasma cells lie at the same level, usually around vessels. The appearances are in keeping with incontinentia pigmenti and no evidence of tinea is seen.

Discussion.—A fixed drug eruption was suggested. But although the child occasionally took a purgative containing phenolphthalein, she says she has not done so for two years. Suppression of all purgatives and tooth pastes has made no difference to the appearance of the rash. An alternative diagnosis put forward was a late-developing naevus.

Postscript.—A provocative dose of phenolphthalein administered at a later date was followed by redness of all the spots within half an hour, vesiculation later the same day, and the appearance of three fresh lesions.

Cat-Scratch Disease.—Dr. Hugh Calvert.

A girl aged 10.

History. During November 1951 the patient developed on her right thigh, about 3 inches below the groin, a little papulo-pustule. A week later she fell downstairs, and for the first time noticed a swelling in her right groin. The papulo-pustule of the thigh, after discharging slightly, became scabby and then healed, leaving a small pigmented scar ; it has remained healed since. The swelling in her groin increased,

and in two places the overlying skin reddened and broke down to form sinuses discharging scanty sero-pus. This discharge has continued intermittently ever since.

The patient herself is in good health, with nothing significant in her past or family history.

There is a healthy cat in the house with which she plays but she has no memory of any scratch.

On examination.—Well-built healthy girl. Palpable in her right groin are some firm tender glands underlying two small sinuses. The skin around the sinus openings is mildly inflamed, scaly and pigmented, but with no suggestion of lupoid tissue on diascopy. Below can be seen the small scar of the initial lesion. No other abnormality found on physical examination.

Investigations.—Chest skiagram normal. Haemoglobin 75%. E.S.R. 3 mm. in 1 hr. Mantoux 1 : 100,000, 1 : 10,000, 1 : 1000, 1 : 100 and 1 : 10, all negative. Cat-scratch antigen 0·1 c.c. intradermally gave a positive result consisting of an inflammatory dermic papule, maximum 72 hours later.

Postscript.—Repeated Mantoux (February 1953) 1 : 10,000, 1 : 1000 and 1 : 100 still negative.

Hypercholesteraemic (Familial) Xanthomatosis. Dr. Hugh Calvert.

A woman aged 58.

History.—The patient is the second child of a family of seven ; the first sibling died in infancy, the third was a stillbirth, the fourth and fifth died as babies, the sixth and seventh were twins, of whom one died as a baby, while the other is alive and well at the age of 54. The patient's husband and three children are alive and well.

The patient has been in excellent health until five years ago. She then began to develop yellowish lumps on the backs of her fingers, elbows and knees, which have continued to increase in size since ; they are not painful, but " tingle ". During the last four years she has had a pain in the back, gradually getting worse but with some recent amelioration. Her appetite is good and she does not suffer from indigestion or flatulence ; she sometimes has nausea but never vomits ; she has never been jaundiced and her bowels are regular. There has been considerable weight loss over the past year but no excessive thirst, nor polyuria, nor frequency. There has been occasional incontinence, and she has noticed that her legs are getting clumsy.

On examination.—A rather obese woman. Numerous pea-sized or larger yellowish nodules on backs of fingers, elbows, knees and buttocks. These have the appearance of typical xanthoma. B.P. 180/95. No abnormalities detected in cardio-vascular or respiratory system. C.N.S. : Cranial nerves normal ; arm reflexes very brisk, with bilateral inverted supinator responses and some loss of power ; exaggerated leg reflexes, extensor plantar responses and bilateral patellar tonus.

Investigations.—Haemoglobin 90%. R.B.C. 5,000,000. W.B.C. 5,300. (Eos. 6%, baso. 2, poly. 32, lympho. 56, mono. 4).

In the stained film the cells are normal.

Glucose tolerance test normal. No evidence of latent diabetes. Blood cholesterol 700 mg./100 c.c. Serum not milky.

Blood Kahn negative.

E.C.G. no abnormality.

Histamine test meal : free HCl present.

Skiagrams.—Skull : pituitary fossa enlarged ; posterior clinoid process decalcified and displaced slightly backwards.

Cervical spine : hypertrophic osteo-arthritic changes C5, 6 and 7 with much lipping and loss of cartilage ; kyphosis at level of C4 and C5.

Lumbar spine : hypertrophic osteo-arthritic changes.

Abdomen : Large Riedl's lobe of liver with no suggestion of enlargement of spleen.

B.M.R.—Plus 48%.

Progress.—The abnormal findings in the C.N.S. were attributed to changes in the cervical spine suitable later for trial with a plaster collar.

Heparin, 25 mg. twice weekly, was given intramuscularly for the hypercholesteraemia.

Blood cholesterol: 700 mg./100 c.c. (24.v.52); 890 mg./100 c.c. (10.vi.52); 575 mg./100 c.c. (8.vii.52); 630 mg./100 c.c. (2.ix.52).

Heparin treatment started 14.x.52: 280 mg./100 c.c. (11.xi.52); 200 mg./100 c.c. (9.xii.52); 375 mg./100 c.c. (6.i.53); 335 mg./100 c.c. (3.ii.53); 445 mg./100 c.c. (3.iii.53); 315 mg./100 c.c. (16.iii.53).

Almost immediately the xanthomata showed signs of regression. Many of them, such as those on the buttock, have completely gone, and all have steadily become smaller.

Pseudoxanthoma elasticum.—Dr. D. S. Wilkinson.

A woman aged 32.

A typical case of this condition with skin changes and angioid streaks. She also suffers from a persistent menorrhagia for which no gynaecological cause has been found. There is no family history of pseudoxanthoma.

Case for diagnosis ? Toxic Nodular Erythema.—Dr. D. S. Wilkinson.

A man aged 72.

This patient has had recurrent erythematous nodular lesions occurring on any part of the body and lasting from three weeks to three months. Biopsy of these lesions shows no specific changes, apart from vascular dilatation, oedema and some mixed cell infiltration. He also has a blood picture consisting of a low haemoglobin (25–60%), and a persistent total leucopenia, the count never rising to more than 3500. Sternal marrow examination showed normal distribution and the presence of free iron. There is no evidence of myelomatosis. The nodules appeared to be partly controlled by arsenic but eventually recurred. The anaemia is presumed to be due to a gradually increasing hypoplasia of the marrow, of unknown cause. The plasma globulin is greatly raised. No drugs are taken and no sepsis has ever been demonstrated.

Postscript.—(May 14). This patient entered hospital again with massive pleural effusion on the left side of the chest and died in a few days. Post-mortem showed old fibro-caseous tuberculosis with terminal miliary spread and an early adenocarcinoma of the prostate.

The following cases also were shown:

Dr. Alice Carleton: **Tuberculosis of Nose, Hard Palate, Feet and Legs; Mycosis Fungoides** *à tumeurs d'emblee*; **Dyskeratosis Follicularis of Darier; ? Lichen Planus of Glans Penis; Spiegler-Fendt Sarcoid; Bullous Lupus Erythematosus of the Mouth with Atrophic Patches on Scalp.**

Dr. Hugh Calvert: **Granuloma Annulare in a Diabetic; Lichen Nitidus; Telangiectasia Eruptiva Perstans of Face; Parapsoriasis; Pili Torti; Atrophic Tuberculoderm; Kyrle's Disease; Guttate Psoriasis.**

Dr. D. S. Wilkinson: **Pili Torti; Epiloia; Naevus Acneiformis Lateris (2 cases); ? Tertiary Lues; ? Lichen Planus; Erythema Gyratum Perstans; Ectodermal Dysplasia; Localized Purpuric Capillaritis; Thrombotic Ulcers of the Feet with Still's Disease and Pancreatitis.**

BOOK REVIEW.

Contact Dermatitis.*

Careful observation of the lesion may provide a clue to the cause of a dermatitis. History-taking, patch-test techniques, and differential diagnoses occupy the first 30 pages of this book, most of the remainder being devoted to the specific patterns produced by contact with a wide variety of objects. The author's material is mainly domestic rather than industrial, but the choice is wide enough to include golf clubs, vacuum cleaners, lawn mowers, bicycles, and even brides and bootlaces.

Accompanying the text are 332 photographs, some showing actual cases, others illustrating specific patterns semidiagrammatically. The majority of the latter are on the hands, and are grouped according to the shape of the object handled. The result is a comprehensive reference album for the specialist, although much of it is likely to be caviare to the general practitioner. The sceptic might be tempted to speculate on the relative parts played by theory and practical experience in the design of some of the patterns. It would have been interesting in this connection to see the pattern made on the dining-room table by the finger nails of the polisher whose hand is illustrated in Figs. 95 and 95A.

The remainder of the book deals with dermatitis affecting special situations, drug rashes, and therapy. The author finds contact dermatitis to be by far the commonest cause of pruritus vulvae, and a very generous space is allotted to the subject of ano-genital pruritus.

It is not easy to produce a short handbook useful for both the general practitioner and the specialist, and there is an inevitable lack of balance in the volume as a whole. Readers, for example, requiring to consult Table III in order to learn the common appearance of psoriasis or pityriasis rosea will derive little help from the rather rigid and elaborate patterns illustrating Chapter 7. Before attempting to diagnose dermatitis caused by grating horse-radishes left-handed it is necessary to know something of cheiropompholyx, pustular psoriasis and acrodermatitis continua.

This volume does not aim at completeness, but the omission of any reference to " textile " or " khaki " dermatitis is surprising, as is the failure to include the striking pattern of dermatitis bullosa striata pratensis among the examples of plant dermatitis. The text, moreover, contains many statements which are controversial or inaccurate ; few dermatologists, for example, will agree that fungus infections are the commonest cause of itching eruptions inside the ear canal (page 53), or that mycosis fungoides can be readily diagnosed by means of a blood-count (page 15).

Apart from the haphazard arrangement of the photographs, the book is well and attractively produced. H. T. H. W.

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* *Contact Dermatitis*. By George L. Waldbott. Springfield, Illinois : Charles C. Thomas. Oxford : Blackwell Scientific Publications. Pp. 232. Illus. 332. Price 63*s*. net.

CURRENT LITERATURE.

ORAL CORTISONE TREATMENT OF INFANTILE ECZEMA. L. W. Hill. (1953) *New Engl. J. Med.*, 248, 1051.

Eighteen eczematous children were given cortisone by mouth in addition to ordinary treatment. Results were " superior in 8, worth-while in 6 and unsatisfactory in 4. The only adverse effects were the development of Cushing's syndrome in one patient and potassium deficiency in another when the dose was too large (150 mg.)."

The initial dose was 75 mg. daily. This was decreased when the disease was controlled. Treatment continued for several months, but never longer than eleven months.

It is recommended that cortisone should be used only in severe cases, and for as short a time as possible. A. D. P.

CAT-SCRATCH DISEASE. F. Ray Bettley and E. A. Fairburn. (1953) *Lancet*, 1, 520.

From the results of intradermal testing of forty controls with the antigen of cat-scratch disease it appears that the intradermal reaction with cat-scratch disease antigen is specific, but positive reactions should be interpreted with care, for they may be obtained in apparently normal people presumably as a result of previously undiagnosed infection. They are therefore of limited value in the diagnosis of an actual present illness. R. H.

TREATMENT OF LUPUS VULGARIS WITH ISONIAZID. Brian Russell, N. A. Thorne and R. V. Grange. (1953) *Lancet*, 1, 964.

This is a preliminary report on the treatment with isoniazid of 15 patients with lupus vulgaris after nine months' experience of using the drug. Those treated by mouth were usually given 300 mg. daily, and those treated by injection into the lesions were given 50–250 mg. weekly. Where both methods were used the oral dosage was 300 mg. daily, and the injected dose up to 400 mg. per week. Apart from mild urticaria in 1 patient there was no intolerance. All the patients except 1 improved, and in most of them this was progressive up to the time of writing. R. H.

ERYTHEMA MULTIFORME EXUDATIVUM MAJOR. D. M. Davies. (1953) *Lancet*, 1, 1126.
STEVENS-JOHNSON SYNDROME TREATED WITH A.C.T.H. W. G. D. Caldwell. (1953) *Lancet*, 1, 1127.
STEVENS-JOHNSON SYNDROME. P. W. Grant. (1953) *Lancet*, 1, 1129.

The authors of these articles report typical cases of this syndrome. Although varying therapeutic measures were used, all cases made the usual recovery, and it is doubtful if any of the drugs used greatly influenced the course of the disease. In correspondence referring to these cases in a later number of the Journal, Dr. Sneddon appeals for a therapeutic investigation into these cases, suggesting that every other case should be treated with A.C.T.H. early in the illness, the remainder being treated with antibiotics. Within a few years sufficient data should be forthcoming to decide the relative values of the varying methods. R. H.

IS SCALP RINGWORM SELF-LIMITING ? C. H. Whittle. (1953) *Lancet*, 2, 10.

In an epidemic of scalp ringworm affecting 13 children in a small village and its school the lesions were difficult to diagnose, atypical, small and very slow in developing. They responded in most cases to simple local applications. X-ray epilation was used in only 4 children. The average duration of treatment to cure was nine months. The organism concerned in all the cases (ten) in which positive cultures were obtained was *M. audouini*, dysgonic form. This is the first epidemic in which this organism has been shown to be the responsible agent. R. H.

AN UNUSUAL ACID-FAST INFECTION OF THE KNEE WITH SUBCUTANEOUS ABSCESS-LIKE LESIONS OF THE GLUTEAL REGION. REPORT OF A CASE WITH A STUDY OF THE ORGANISM MYCOBACTERIUM ABSCESSUS, n. sp. M. Moore and J. B. Frerichs. (1953) *J. invest. Derm.*, 20, 133.

At the age of 14 the patient while working on a farm injured her left knee and dislocated the patella (it doesn't say if the skin was broken). Though it did not interfere with locomotion some

discomfort persisted until, 49 years later, a sudden exacerbation of pain and swelling demanded synovectomy and arthrodesis. Material removed contained acid-fast bacilli (it doesn't say if they were particularly numerous), and, in spite of negative guinea-pig, the diagnosis of tuberculosis stood until on removal of the plaster abscesses were found in the left buttock, appeared a month later on the right side, and continued to develop for 18 months. A guinea-pig-negative acid-fast bacillus was cultured from the pus.

Then follows 17 pages—not including those occupied by photographs—of bacteriology which the reviewer hasn't read.

The literature contains accounts of granuloma with lymph-node involvement following scratches sustained in swimming-pools, and of small children with pneumonia in whom acid-fast bacilli distinct from the tubercle bacillus were found. J. H. T. D.

THE EFFECT OF COLD-STRESS, A.C.T.H., CORTISONE, PYROGEN AND NITROGEN MUSTARD ON TISSUE MAST CELLS IN THE SKIN AND SUBCUTANEOUS TISSUES OF THE RAT. E. P. Schoch and D. Glick. (1953) *J. invest. Derm.*, **20**, 119.

For the study of mast cells the thin web of subcutaneous areolar tissue is the best. Only nitrogen mustard had any effect on them. The question whether mast-cell granules contain heparin or other hyaluronidase-inhibiting principle continues to exercise great minds.

J. H. T. D.

HISTOPATHOLOGIC STUDIES OF PIGMENTED NAEVI IN CHILDREN. O. C. Stegmaier and H. Montgomery. *J. invest. Derm.*, **20**, 51.

Permission was obtained to remove moles from 98 of 450 prepubertal inmates of a home for the feeble-minded. Twenty-four out of 100 specimens came from the hands or feet; 3 of these were less than 2 mm. in diameter and contained no naevus cells; 2 other pigmented lesions had no naevus cells and were thought not to have been moles. Of the remaining 95 specimens considered satisfactory, 14 had no naevus cells and were classified as lentigo, 47 were junction naevi, 34 combined junction and dermal; no purely dermal naevi and no blue naevi.

Inflammatory changes were seen in 2 cases and mitoses in one only. In none were seen the very large naevus cells believed to be characteristic of malignancy. This study does not deny the existence of malignant melanoma in childhood with metastasis and death before puberty; but it indicates that many features of a mole, commonly regarded by pathologists without dermatological experience, as malignant, are of regular occurrence in childhood.

J. H. T. D.

WATER-SOLUBLE VITAMINS IN NORMAL HUMAN SKIN. T. H. Lee, A. B. Lerner and R. J. Halberg. (1953) *J. invest. Derm.*, **20**, 19.

The assay of B_{12}, riboflavin, ascorbic, folic, nicotinic and pantothenic acids, biotin and thiamine in the skin is described with full detail of method, and the results are compared with the published values for other organs.

The water-soluble vitamin content seems to be lower in the skin and mammary gland than anywhere else in the body—hence, no doubt, the popularity of the herbalist, both crypto- and phanero-. J. H. T. D.

A NOTE ON FINGER-NAIL GROWTH. W. B. Bean. (1953) *J. invest. Derm.*, **20**, 27.

The rate of growth does not vary with the season but it slows down as we get older.

J. H. T. D.

STUDIES ON SKIN-HYPERSENSITIVITY TO LANOLIN. M. B. Sulzberger, T. Warshaw and F. Herrmann. (1953) *J. invest. Derm.*, **20**, 33.

During a year, patch tests with anhydrous lanolin U.S.P. were applied in standard fashion to unaffected skin of 1048 (? consecutive) patients who were attending the section of allergy (? as new patients or chronic cases) "because of various dermatologic ailments." Twelve of them gave positive reactions. The control series, of 120 healthy volunteers, was hardly big enough with a morbidity of only 1·17%: though it would depend of course on what sort of volunteers they were. Persons volunteering to assist a stage hypnotist for example would of course do much better than this.

Besides these 12 there were 7 patients previously discovered to be allergic to lanolin. Of the

19, 16 were females. None of them reacted to the inunction of lanolin, though one or two had their dermatosis made worse by it (" What you don't put on don't give no trouble ").

Infinite pains were taken to break the lanolin down into its constituents, and the attempt was made to render certain " mixed lanolin alcohols " harmless by acetylation. J. H. T. D.

STUDIES OF THORIUM X APPLIED TO HUMAN SKIN. II : COMPARATIVE FINDINGS OF THE PENETRATION AND LOCALIZATION OF THORIUM X WHEN APPLIED IN ALCOHOLIC SOLUTION IN OINTMENT AND IN LACQUER VEHICLES. V. H. Witten, M. S. Ross, E. Oshry and V. Holmstrom. (1953) *J. invest. Derm.*, **20**, 93.

It is worth knowing that the thorium X is initially dissolved in water. So if you use lacquer be careful to shake the bottle, otherwise the thorium gets left behind in the dregs.

J. H. T. D.

SCRATCHING PATTERNS. I : INFLUENCE OF SITE. T. Cornbleet. (1953) *J. invest. Derm.*, **20**, 105.

The author attempts to show that the average length of stroke in a paroxysm of scratching is determined not so much by considerations of accessibility, the mechanics of linear motion along curved surfaces, or economy of effort, as by the prevalence of tactile nerve-endings. Just as the radius of a planetary orbit must sweep equal areas in equal periods of time, so must the patient's nails harrow an equal number of nerve-endings for each quantum of itch-relief.

Tables are given showing the average lengths of excoriation and the threshold distance apart of separable tactile sensations for the different parts of the body ; but their correspondence item for item is not accurate. The most scratched item of all—the head, whether in pityriasis, pediculosis or perplexity—is left out altogether. Then what about that comprehensive school of pruritic studies the anogenital region, where itching may radiate from a point poor in epicritic tactile sensibility to another intensely sensitive to tickle ? Are we to postulate a two-stroke or perhaps a triple-expansion type of mechanism ? There are, moreover, notable discrepancies, namely long scratches on the forearms and legs where the epicritic faculty is pretty high. Surely most of us scratch as scratch can. J. H. T. D.

STUDIES ON THE SULPHYDRYL CONTENT OF THE SKIN. E. J. Van Scott, S. Rothman and C. R. Greene. (1953) *J. invest. Derm.*, **20**, 111.

Sulphydryl compounds found in aqueous extracts of human epidermis inhibit the tyrosinase function in melanogenesis. Inflammatory processes oxidize or otherwise neutralize the -SH-groups, thereby releasing the enzyme.

In 2 patients with pemphigus there was between seven times and twice as much -SH in the normal as in the pigmented skin : and in vitiligo from half as much again to twice as much (in a negro three times as much) as in the normal.

It is here assumed that the pigmented areas in the pemphigus cases were the sites of healed bullae : but is this always the case ? At any rate in dermatitis herpetiformis, in which pigmentation is much more frequent than in pemphigus, it very often looks as if the pigmentary lesion is merely an alternative form of reaction—maybe to some disturbance in the metabolism of -SH-containing protein. But whatever ACTH does in pemphigus it is clear from these studies that it has nothing to do with sulphydryl. J. H. T. D.

PERIPHERAL VASCULAR FAILURE AS CAUSE OF DEATH IN GENERALIZED EXFOLIATIVE DERMATITIS K. Steiner and L. D. Grayson. (1953) *J. Amer. med. Ass.*, **151**, 1479.

Irreversible peripheral circulatory collapse occurred in 4 patients with generalized exfoliative dermatitis. Degenerative changes in the suprarenal cortex were found in 3 cases which came to autopsy. Suprarenal failure is believed to be responsible for the peripheral circulatory failure and extensive infections probably contributed to the resistance to therapy. In 2 of the cases repeated use of cortisone and corticotropin could also have been responsible for the failure of the suprarenals. If these hormones are given in exfoliative dermatitis the dosage should be as low as possible, and it is probably wise to avoid a second course. A. J. R.

ATYPICAL TUBERCULIN REACTIONS. L. S. Arany. (1953) *J. Amer. med. Ass.*, **152**, 491.

In 6 cases of active tuberculosis atypical tuberculin reactions were noted—a large area of erythema and a small area of infiltration after 24 hours, fading completely in 48 hours.

This is often regarded as a false positive reaction, but it may occur in certain phases of active tuberculosis and should be interpreted with caution. A. J. R.